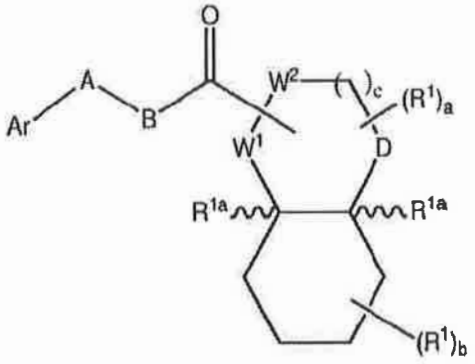
CLAIMS

1. A compound of formula (I):



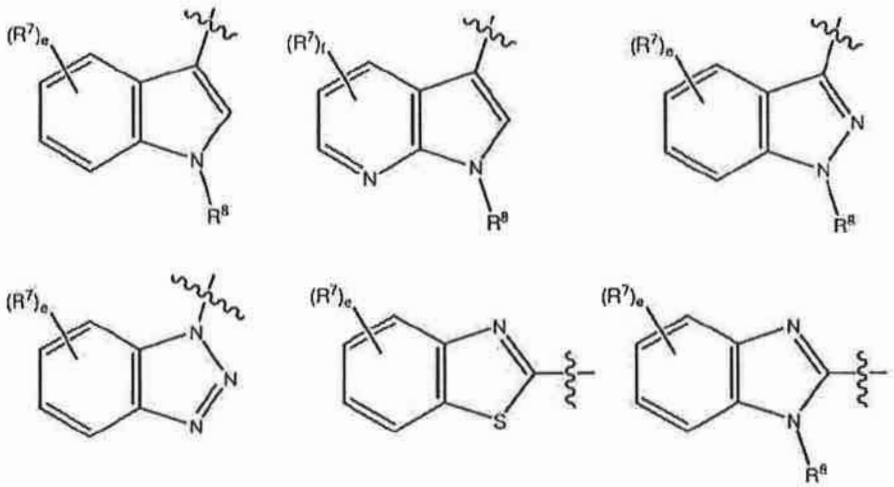
Formula (I)

wherein:

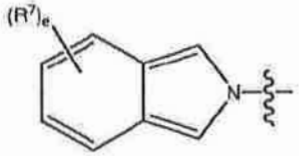
each R^1 and R^{1a} is independently selected from the group consisting of H, methyl, $CONHC(CH_3)_3$, OH, CO_2H, CO_2CH_3, $CO_2CH_2CH_3$, phenyl, CH_2OH, CN, tetrazole and OCH_3[[.]],

or any two R^1 on adjacent carbon atoms may be joined to form a cyclic moiety, or any two R^1 on the same carbon when taken together may form a group of the formula =O;

Ar is an optionally substituted C_1-C_{18}heteroaryl group selected from the group consisting of:



and



wherein each R^7 is independently selected from the group consisting of H, halogen, OH, NO_2, CN, SH, NH_2, CF_3, OCF_3, C_1-C_{12}alkyl, C_1-C_{12}haloalkyl, C_2-C_{12}alkenyl, C_2-C_{12}alkynyl, C_2-C_{12}heteroalkyl, C_3-C_{12}cycloalkyl, C_3-C_{12}cycloalkenyl, C_2-C_{12}heterocycloalkyl, C_2-C_{12}heterocycloalkenyl, C_6-C_{18}aryl, C_1-C_{18}heteroaryl, C_1-C_{12}alkyloxy, C_2-C_{12}alkenyloxy, C_2-C_{12}alkynyloxy, C_2-C_{10}heteroalkyloxy, C_3-C_{12}cycloalkyloxy, C_3-C_{12}cycloalkenyloxy, C_2-C_{12}heterocycloalkyloxy, C_2-C_{12} heterocycloalkenyloxy, C_6-C_{18}aryloxy, C_1-C_1 heteroaryloxy, C_1-C_{12}alkylamino, SR^9, SO_3H, $SO_2NR^9R^{10}$, SO_2R^9, $SONR^9R^{10}$, SOR^9, COR^9, COOH, $COOR^9$, $CONR^9R^{10}$, NR^9COR^{10}, NR^9COOR^{10}, $NR^9SO_2R^{10}$, $NR^9CONR^9R^{10}$, NR^9R^{10}, and acyl;

wherein R^8 is selected from the group consisting of H, C_1-C_{12}alkyl, C_2-C_{12}alkenyl, C_2-C_{12}alkynyl, C_2-C_{12}heteroalkyl, C_3-C_{12}cycloalkyl, C_2-C_{12}heterocycloalkyl, C_6-C_{18}aryl, C_1-C_{18}heteroaryl, SO_3H, $SO_2NR^9R^{10}$, SO_2R^9, $SONR^9R^{10}$, SOR^9, COR^9, COOH, $COOR^9$, and $CONR^9R^{10}$;

wherein each R^9 and R^{10} is independently selected from the group consisting of H, C_1-C_{12}alkyl, C_2-C_{10}heteroalkyl, C_1-C_{12}haloalkyl, C_3-C_{12}cycloalkyl, C_6-C_{18}aryl, and C_1-C_{18}heteroaryl;

e is an integer selected from the group consisting of 0, 1, 2, 3 and 4;

f is an integer selected the group consisting of 0, 1, 2, and 3;

A is $-CR^aR^b-$;

B is CH_2;

wherein each R^a and R^b, is independently selected from the group consisting of H, halogen, OH, NO_2, CN, SH, NH_2, CF_3, OCF_3, C_1-C_{12}alkyl, C_2-C_{10}heteroalkyl, C_1-C_{12}haloalkyl, C_3-C_{12}cycloalkyl, C_6-C_{18}aryl, C_1-C_{18}heteroaryl; SR^2, SO_3H, $SO_2NR^2R^3$, SO_2R^2, $SONR^2R^3$, SOR^2, COR^2, COOH, $COOR^2$, $CONR^2R^3$, NR^2COR^3, NR^2COOR^3, $NR^2SO_2R^3$, $NR^2CONR^2R^2$, NR^2R^3, and acyl and further wherein R^a and R^b are different;

wherein each R^2 and R^3 is independently selected from the group consisting of H, C_1-C_{12}alkyl, C_2-C_{10}heteroalkyl, C_1-C_{12}haloalkyl, C_3-C_{12}cycloalkyl, C_6-C_{18}aryl, and C_1-C_{18}heteroaryl;

W^1 and W^2 are selected such that one is N and the other is (CR^1_2),

the bond from the carbonyl carbon is joined to whichever of W^1 or W^2 is N,

D is (CR^1_2),

n is an integer selected from the group consisting of 0, 1, and 2;

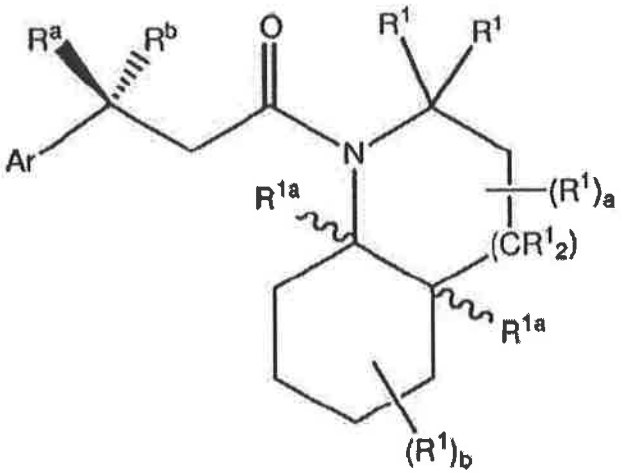
a is an integer selected from the group consisting of 0, 1, 2, and 3 ;

b is an integer selected from the group consisting of 0, 1, 2, 3, 4, 5, 6, 7, and 8,

c is 1;

or a pharmaceutically acceptable salt thereof.

2. A compound according to claim 1 having the formula:



wherein Ar, R^a, R^b, R^1, R^{1a}, a and b are as defined in claim 1.

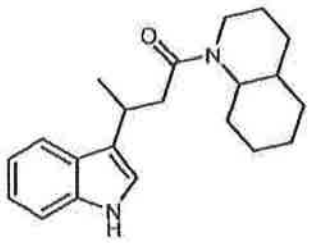
3. A compound according to claim 2 wherein one of R^a and R^b is H and the other is optionally substituted alkyl.

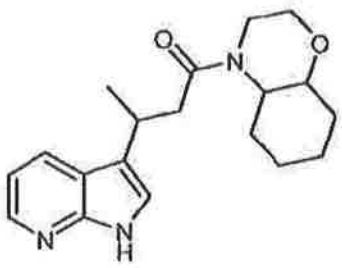
4. A compound according to claim 1 wherein the R^7 substituent is located in the 4 or the 5 position of the six membered ring.

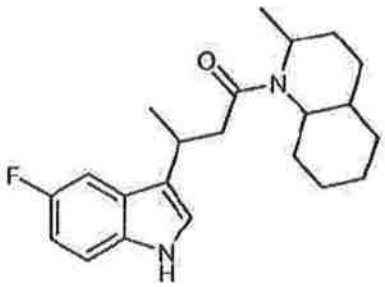
5. A compound according to claim 1 wherein R^7 is selected from

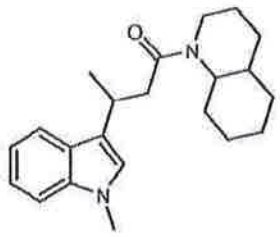
the group consisting of CH_3, CH_2CH_3, $CH_2CH_2CH_3$, $CH(CH_3)_2$, $(CH_2)_3CH_3$, Cl, Br, F, I, OH, NO_2, NH_2, CN, SO_3H, OCH_3, $OCH_2CH_2CH_3$, CF_3, and OCF_3.

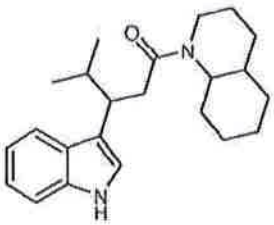
6. A compound according to claim 1 selected from the group consisting of:

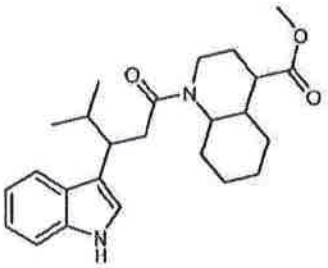


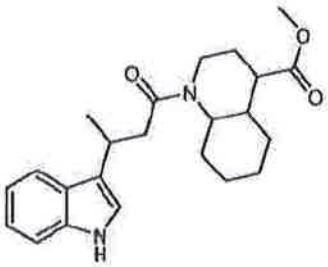


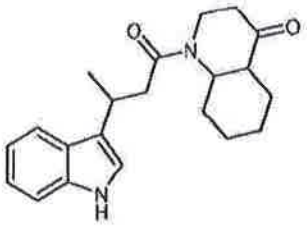


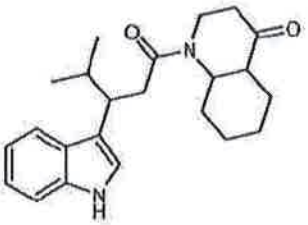


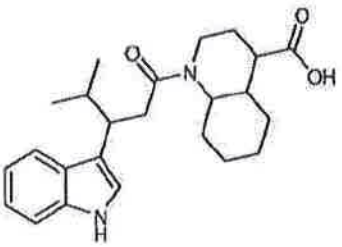


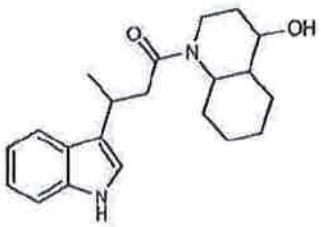


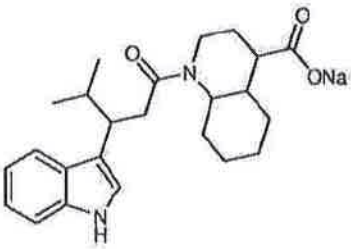


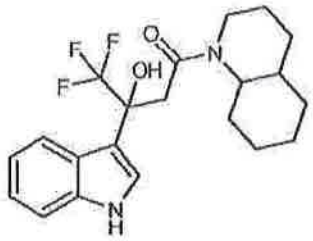


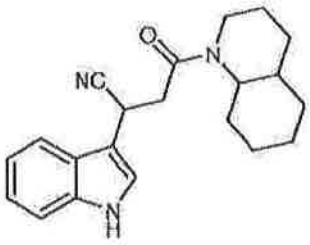


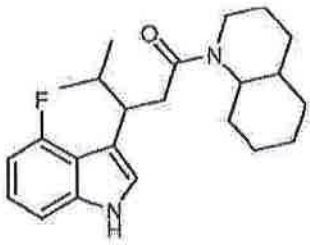


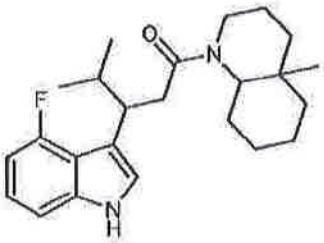


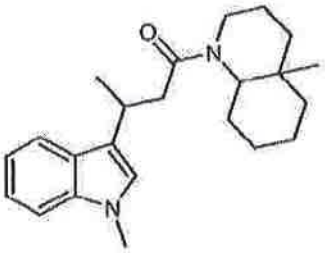


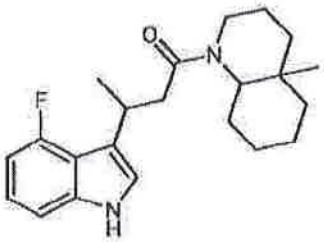


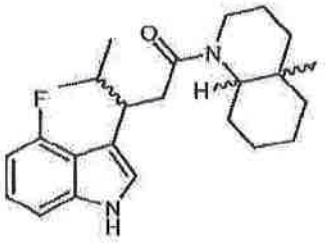


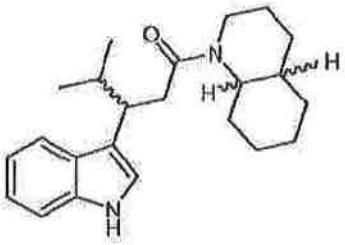


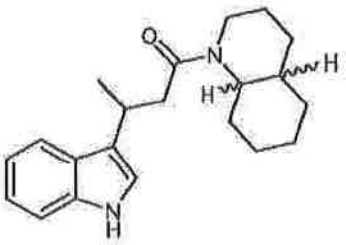


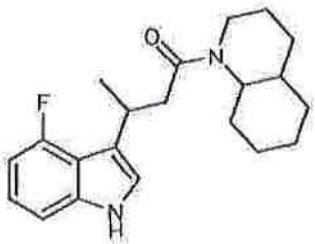


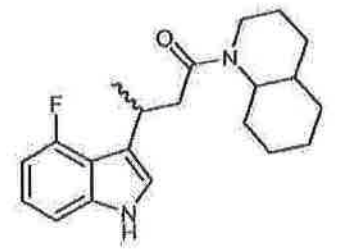


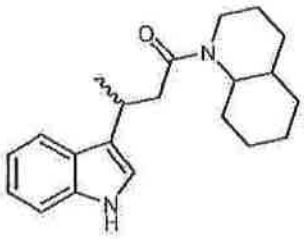


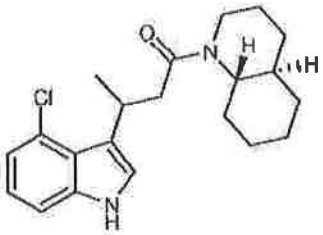


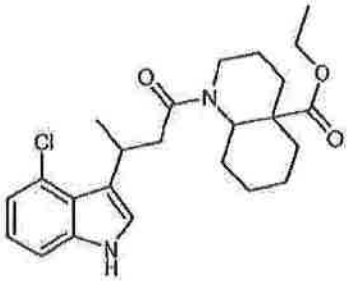


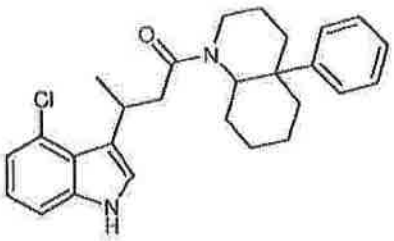


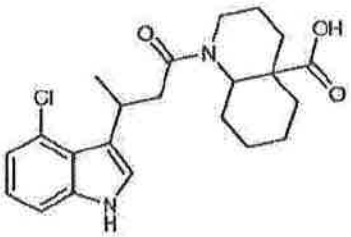


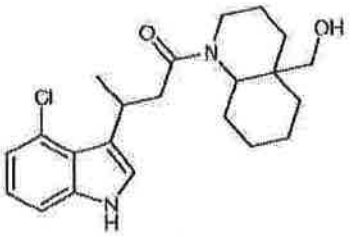


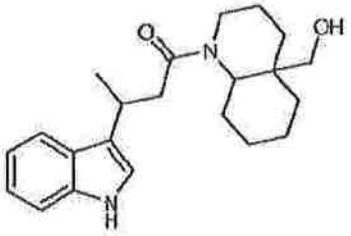


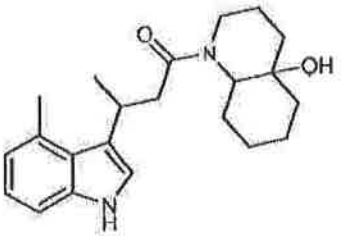


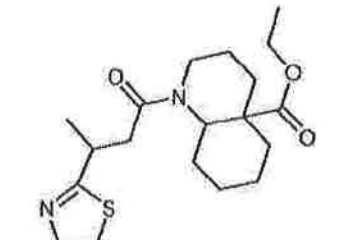


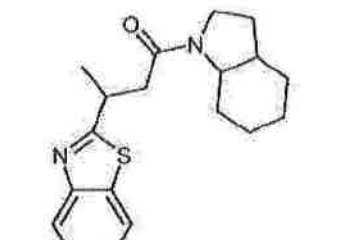


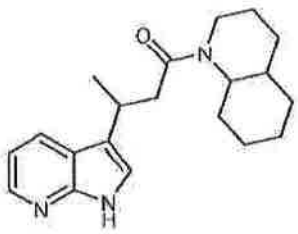


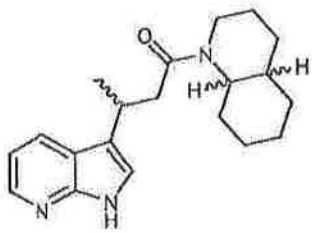


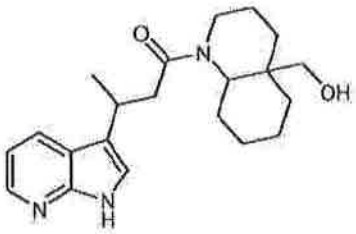


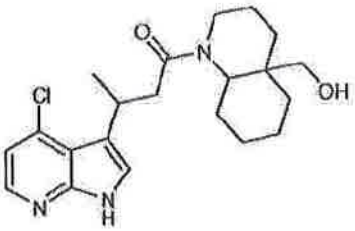


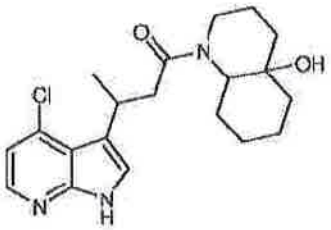


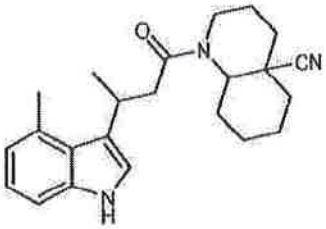


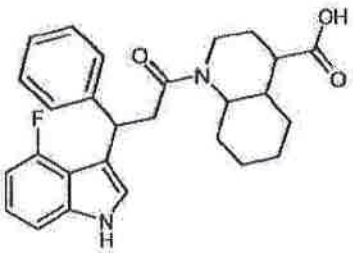


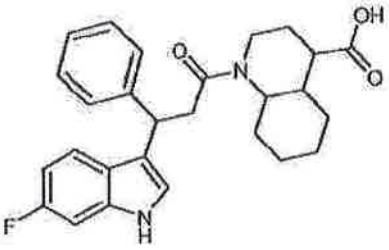


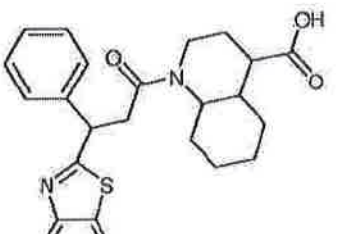




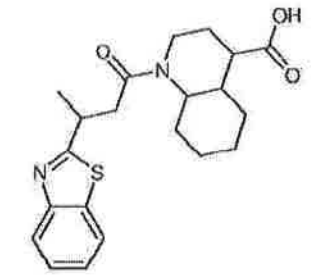


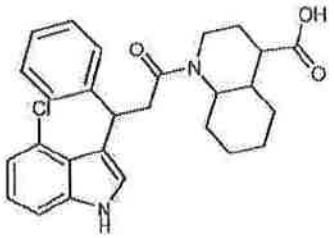


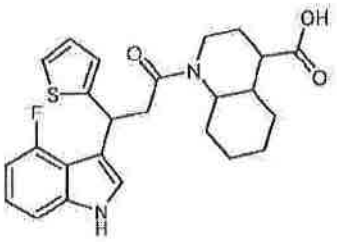


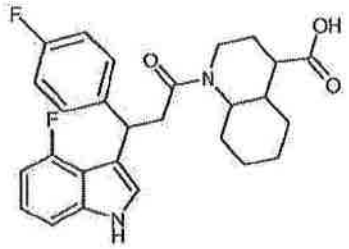


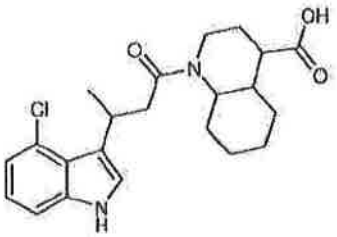


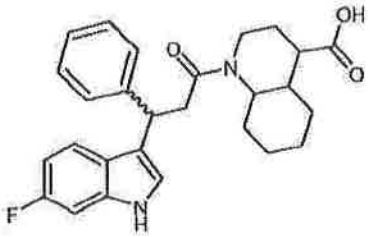


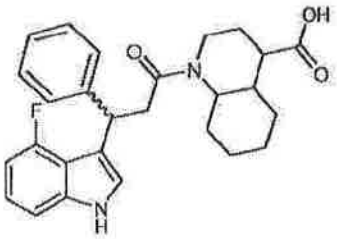


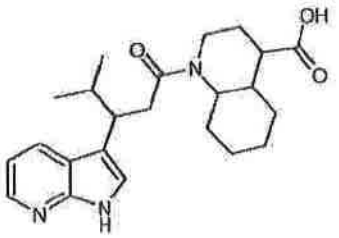


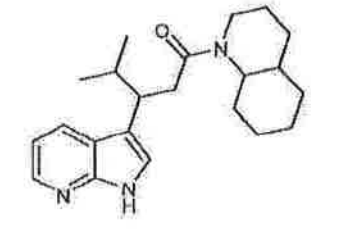


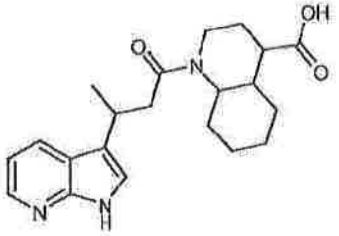


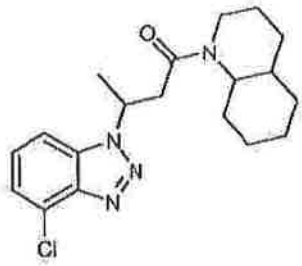


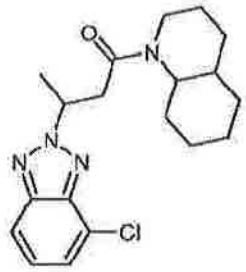


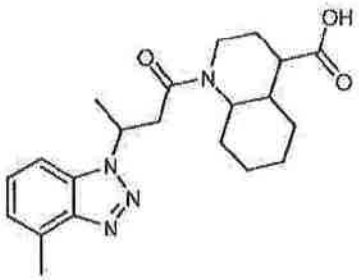


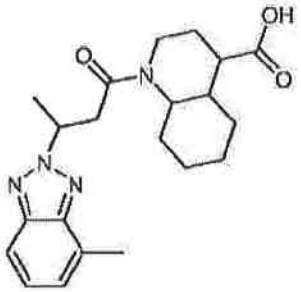


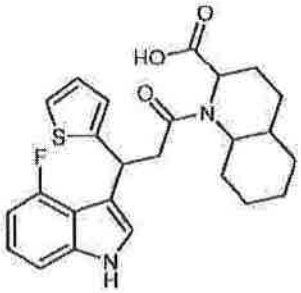


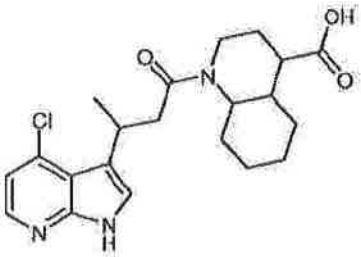


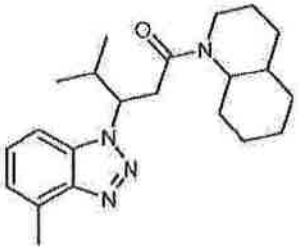


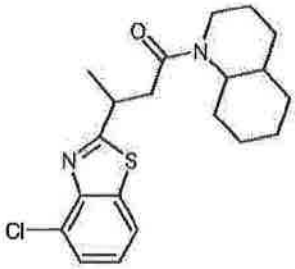


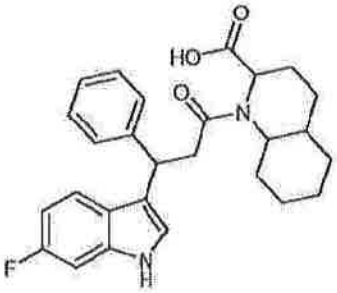


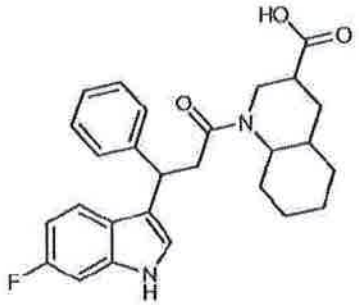








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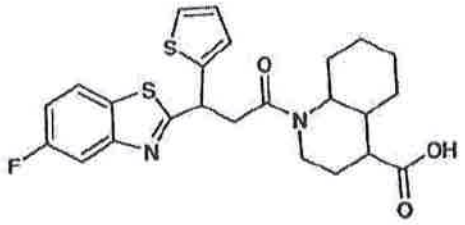
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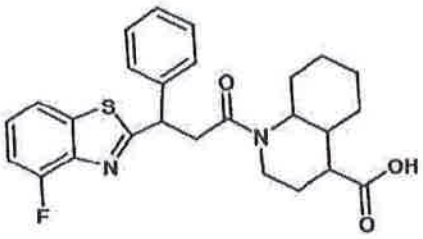
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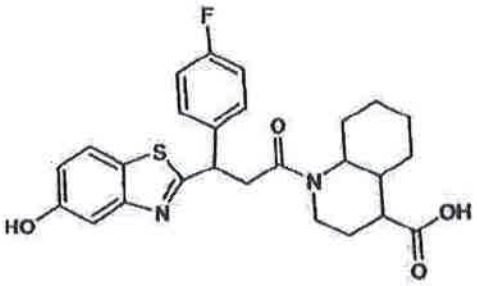
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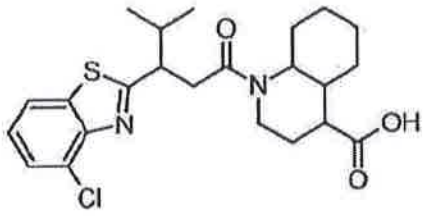
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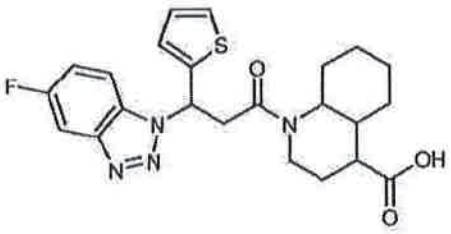
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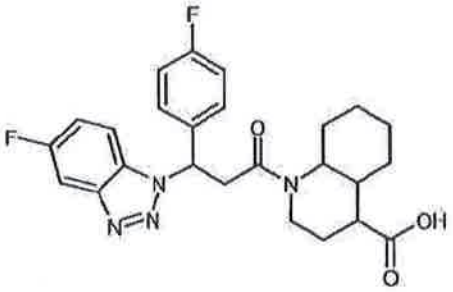
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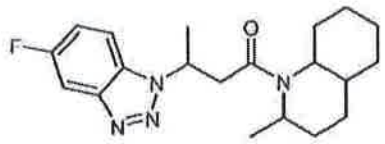

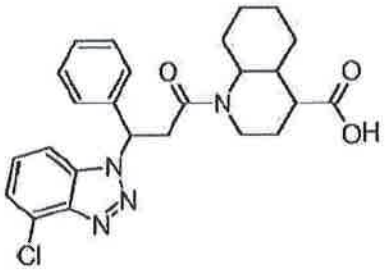

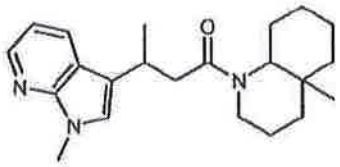



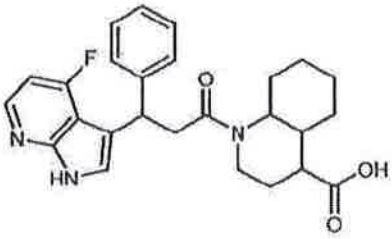

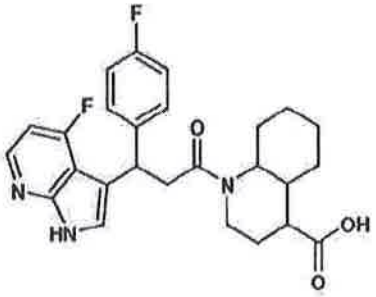

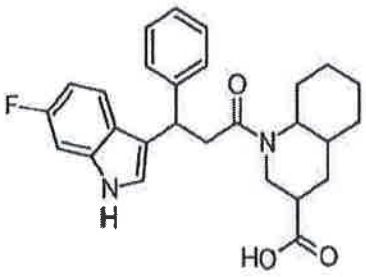

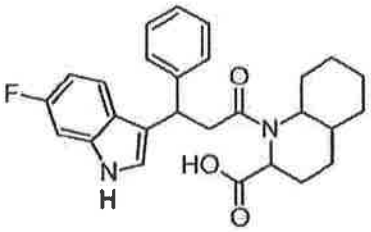



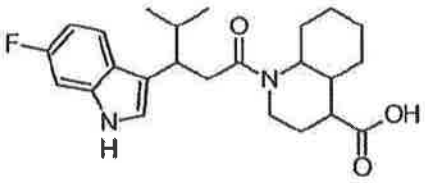

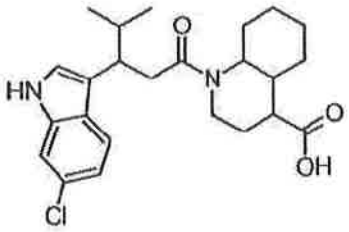

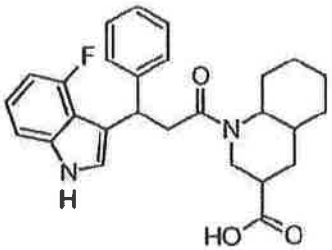

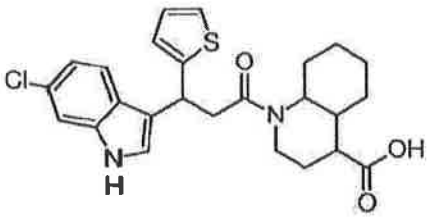

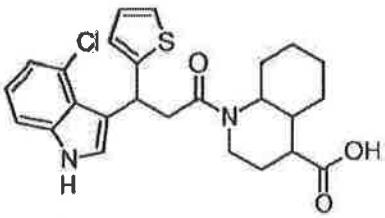

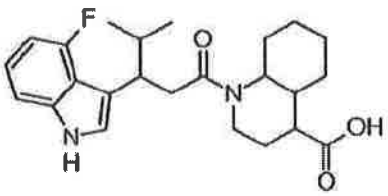

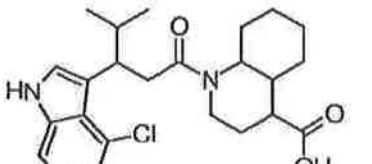

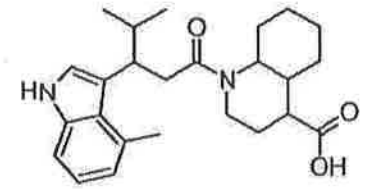


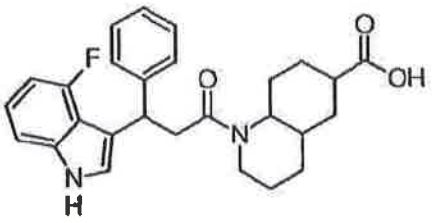
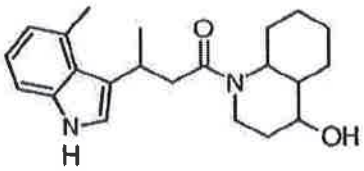
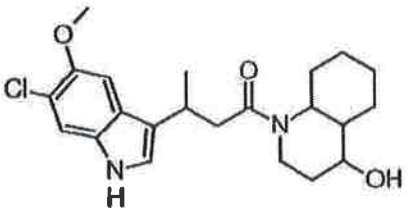
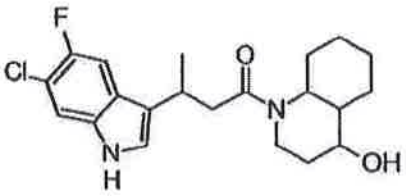
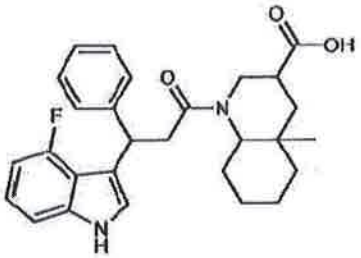
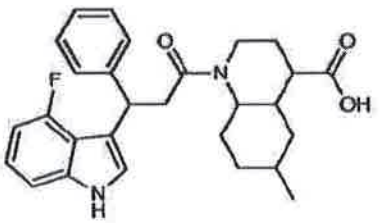
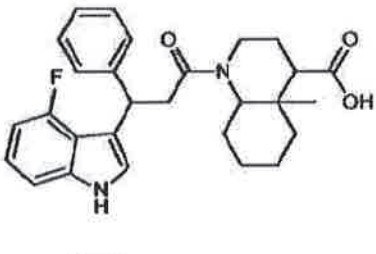
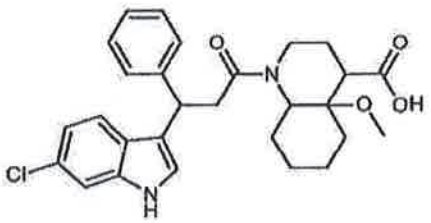
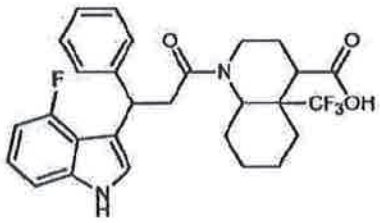

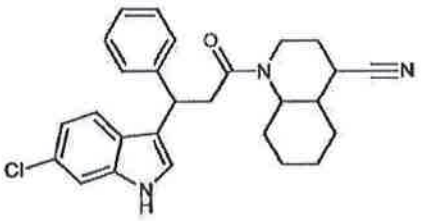

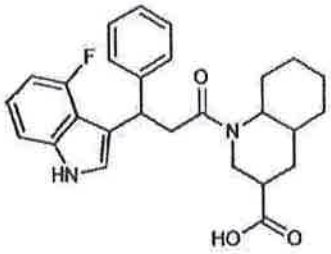

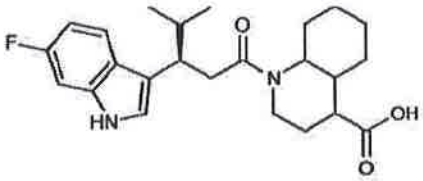

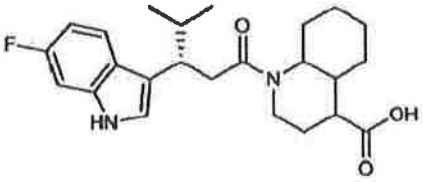

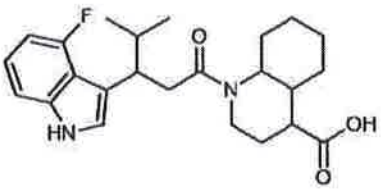

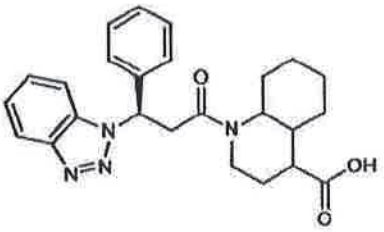

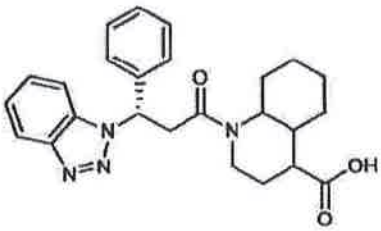

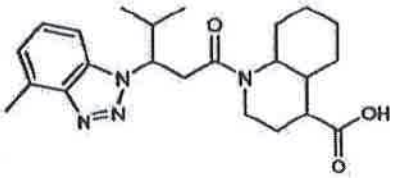

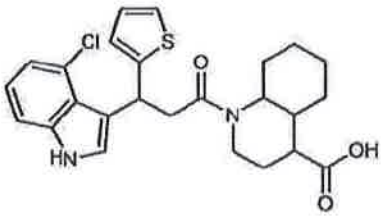

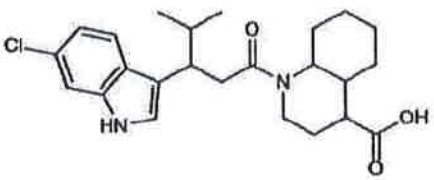

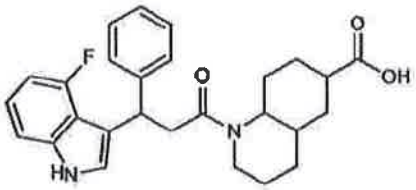

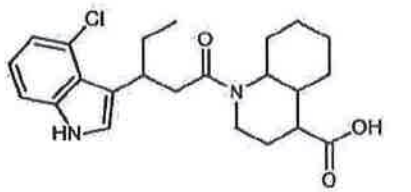

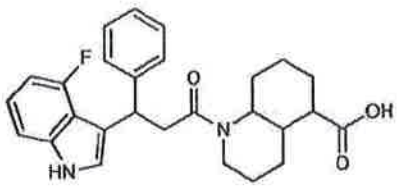
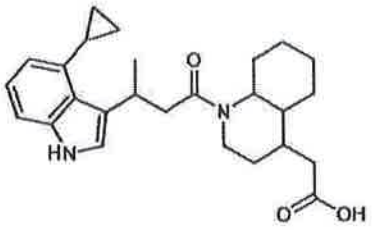
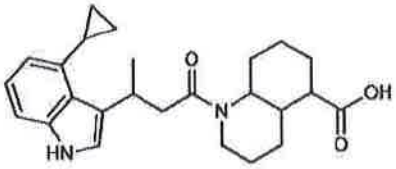
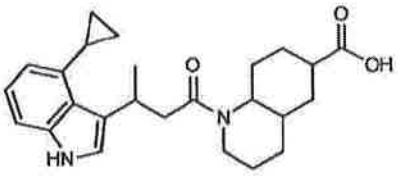
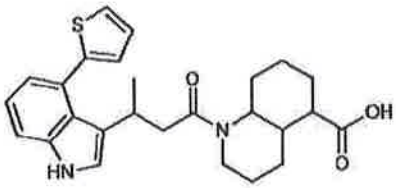
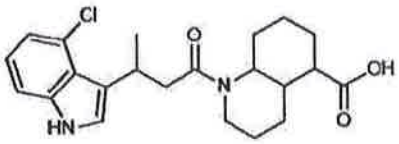
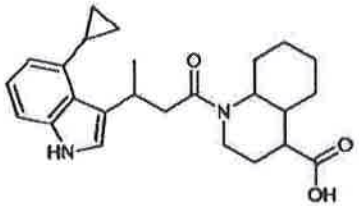
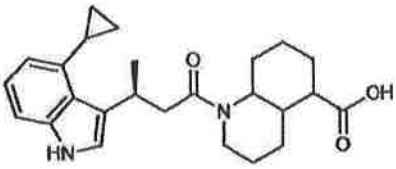
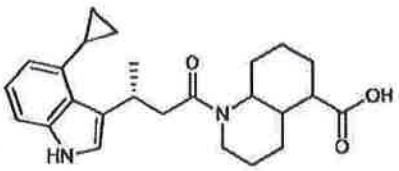
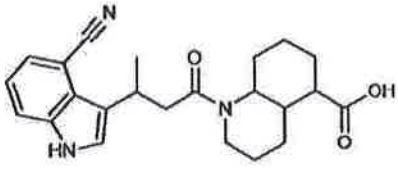
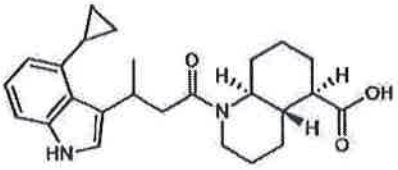
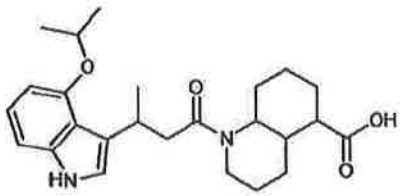

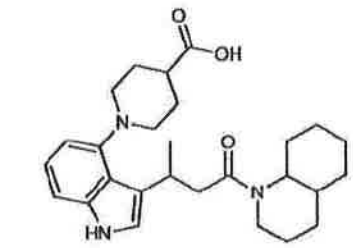

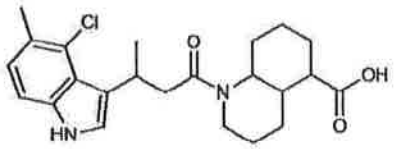

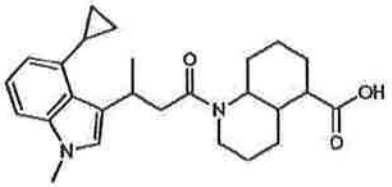

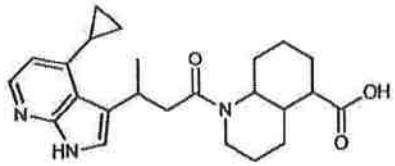

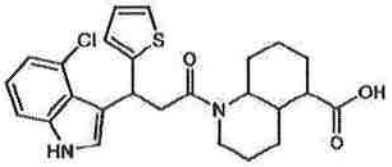

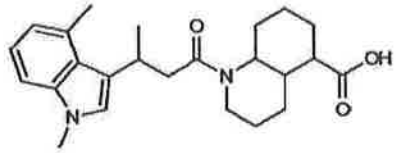

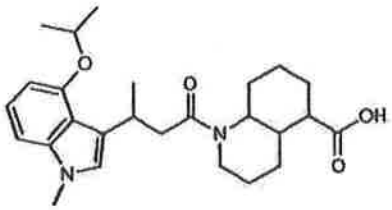

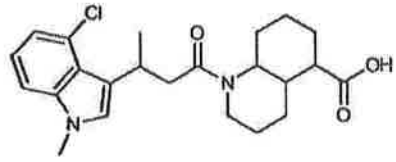

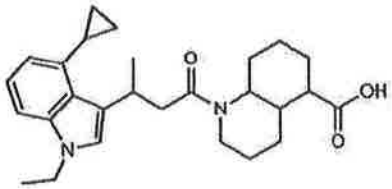

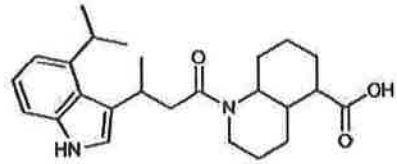

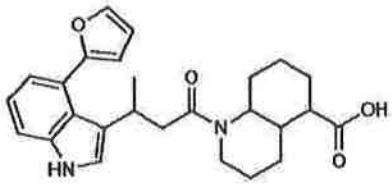

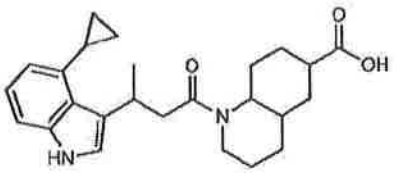

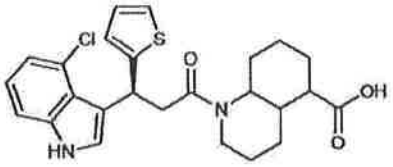

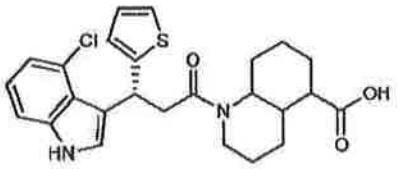

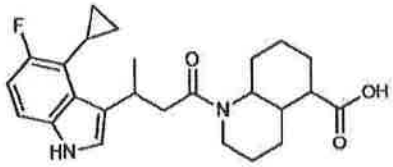

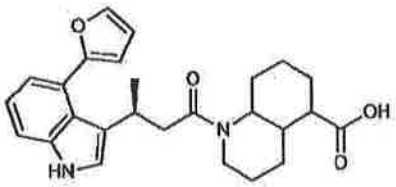

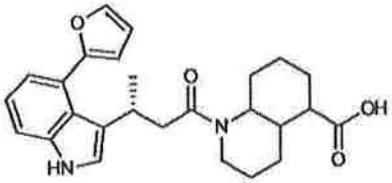

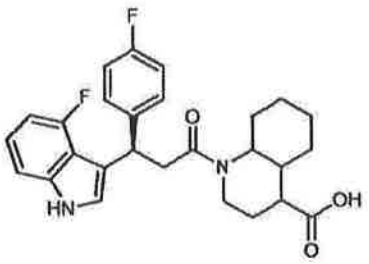

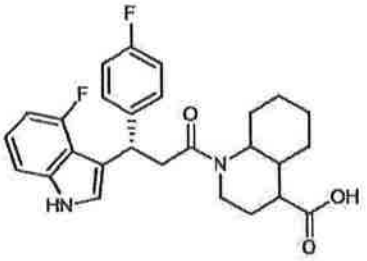

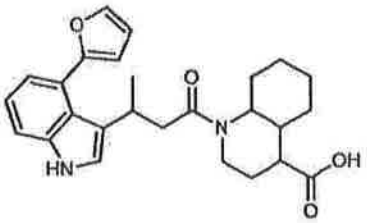

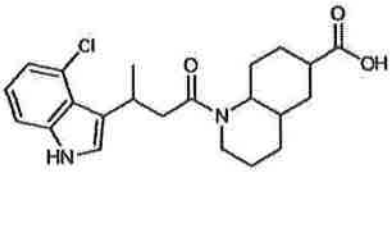

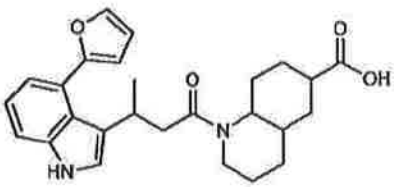

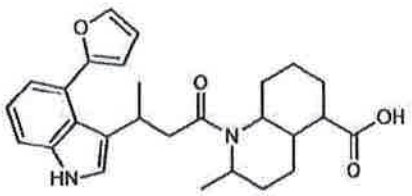

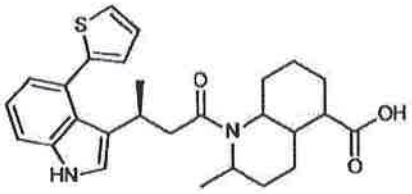

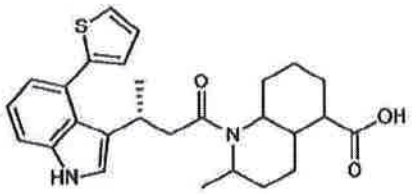

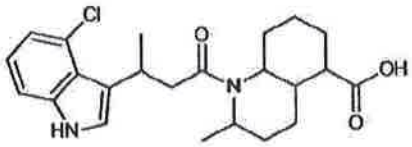

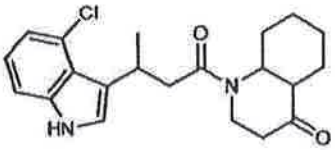

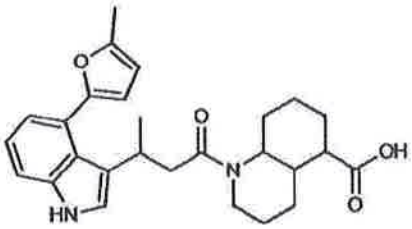

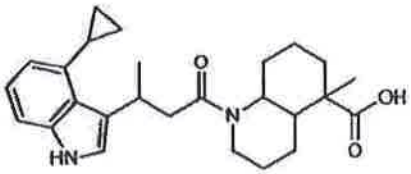

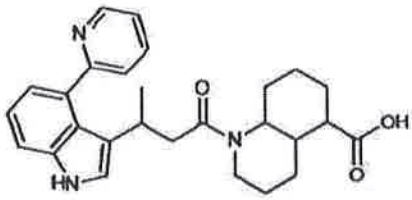

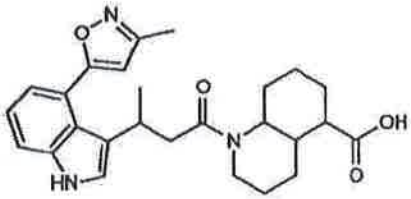

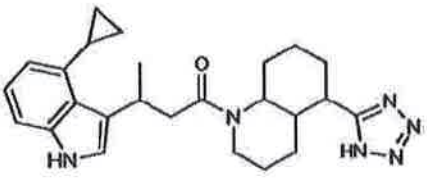

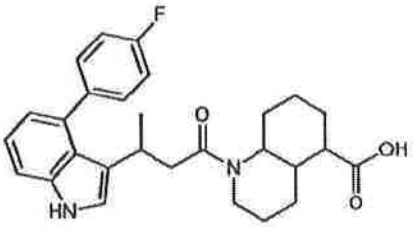

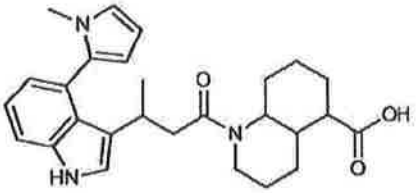

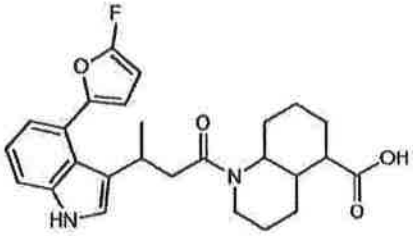

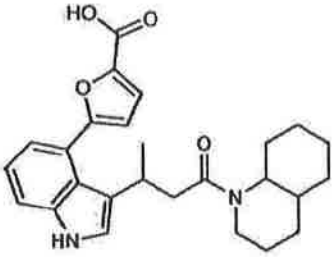

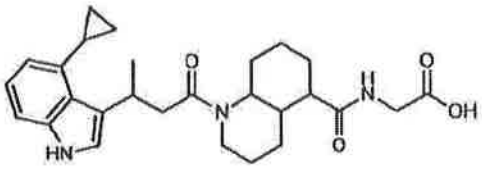

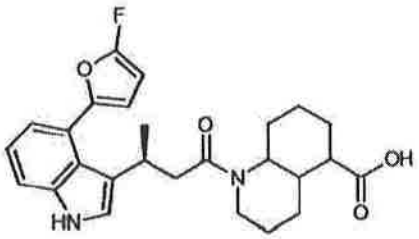

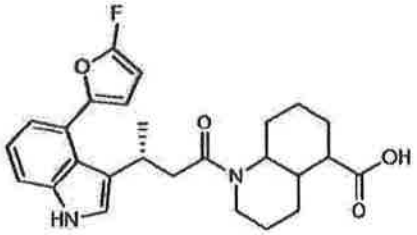

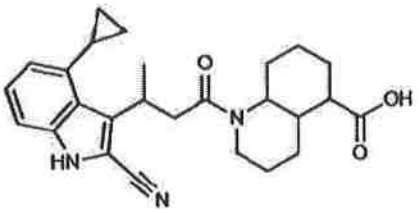

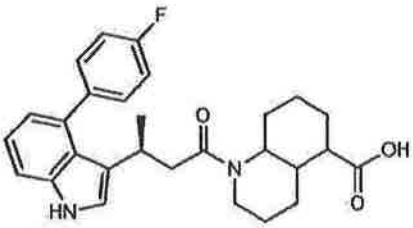

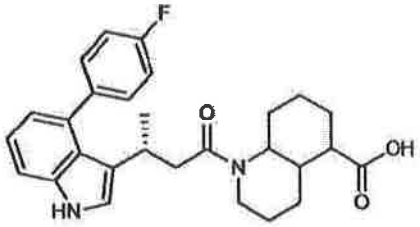

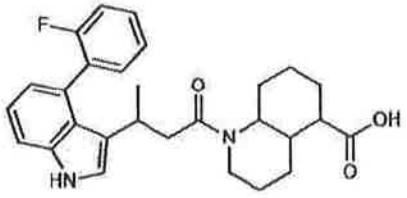
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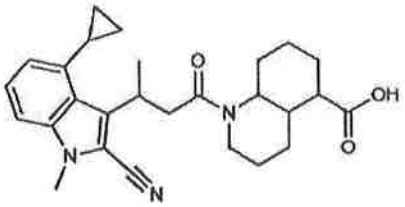
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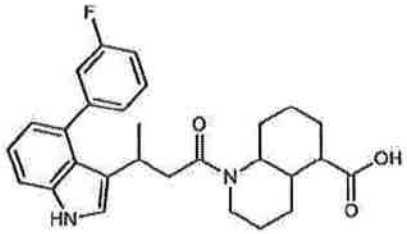
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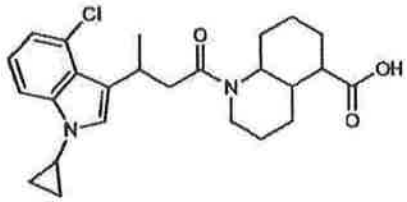
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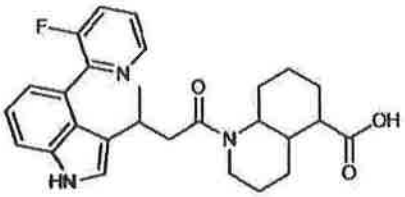
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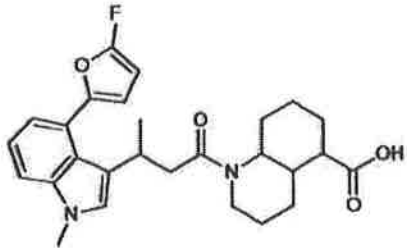
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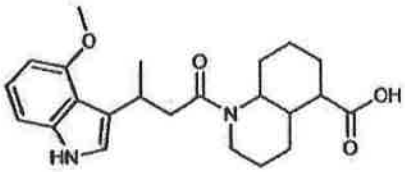
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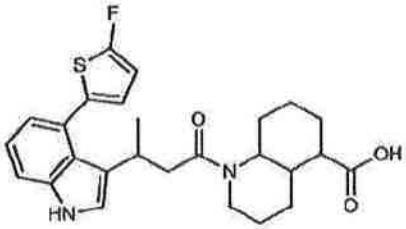
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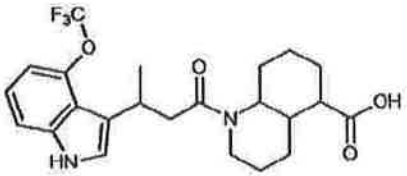
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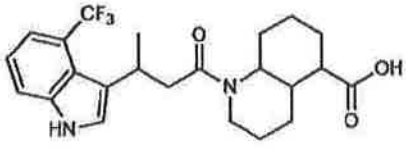
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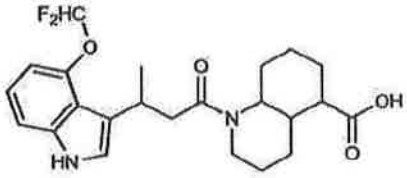
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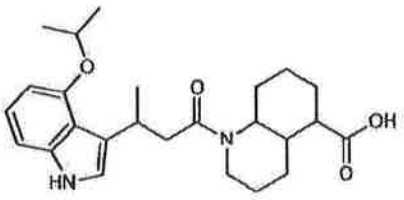

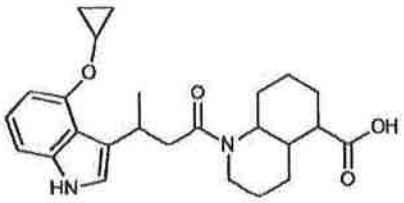

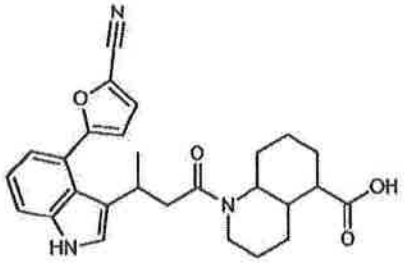

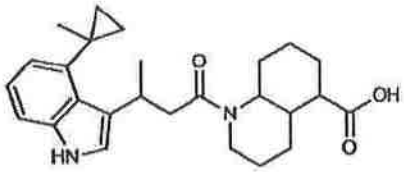

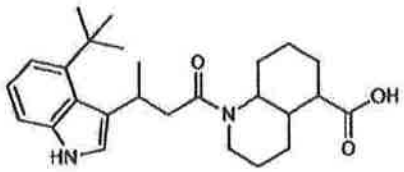

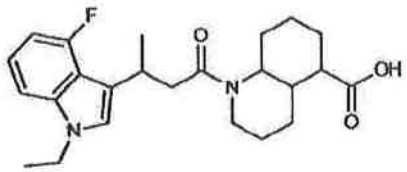

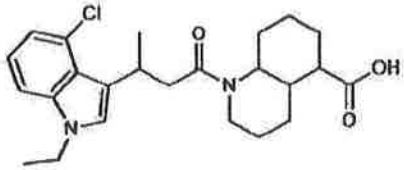

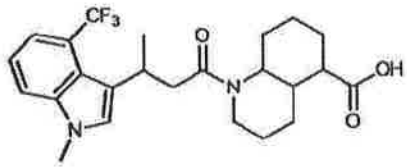

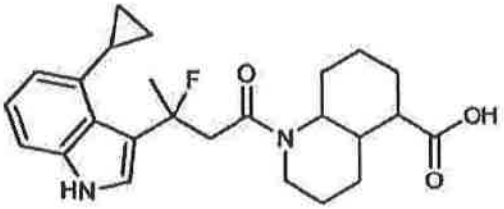



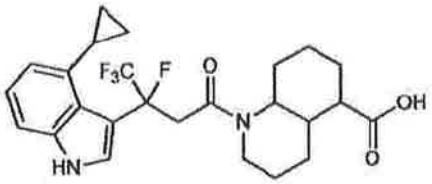

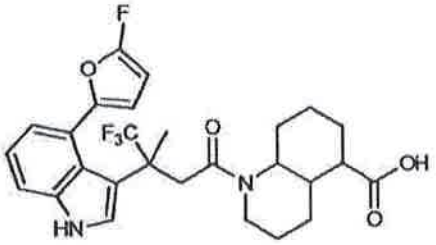





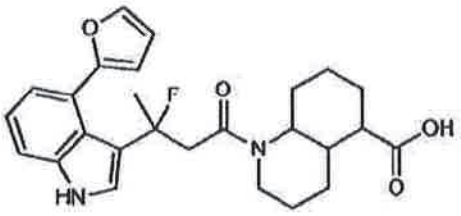

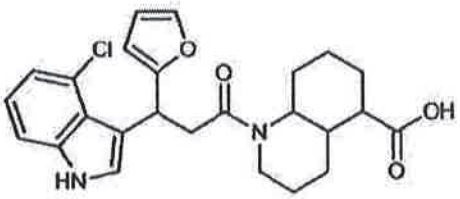



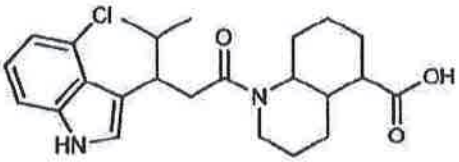

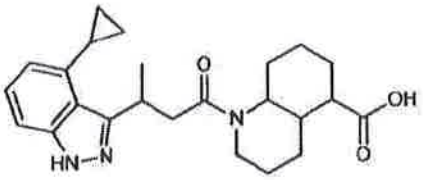

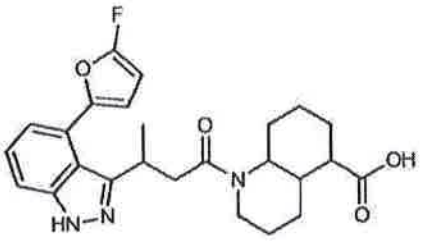



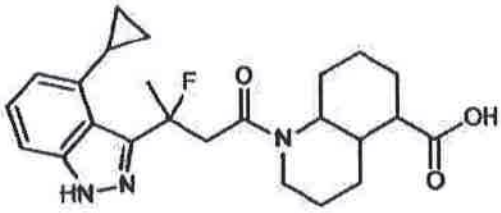

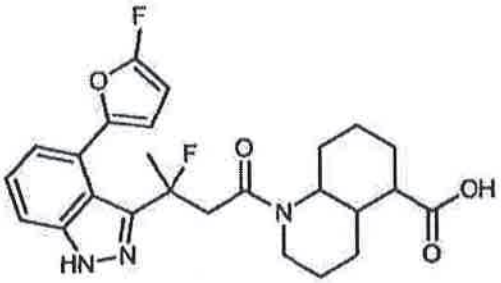



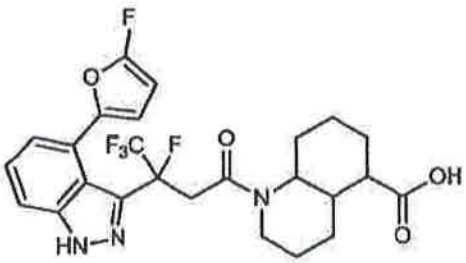

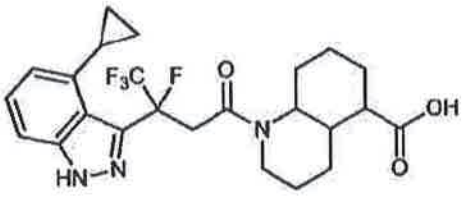

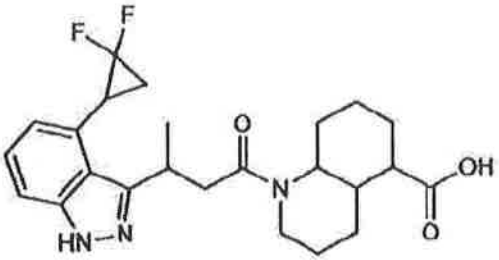

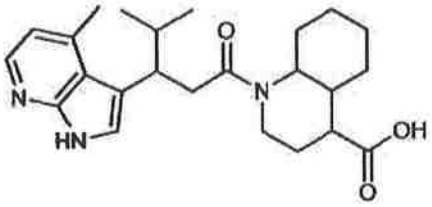

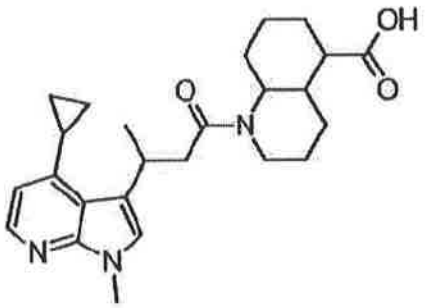

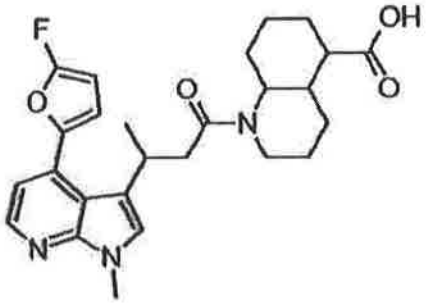

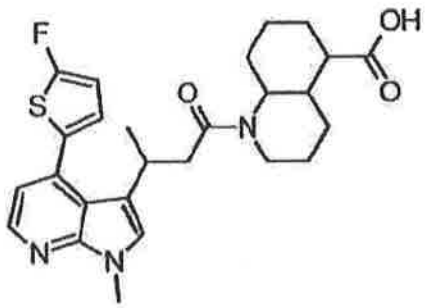

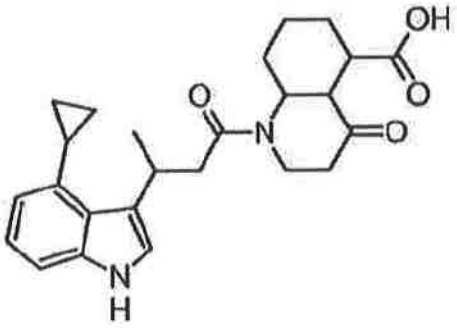

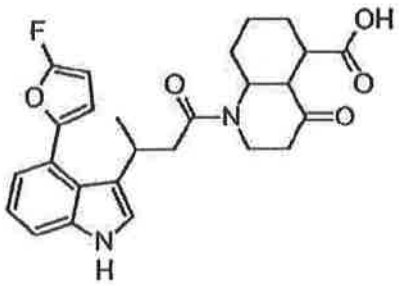

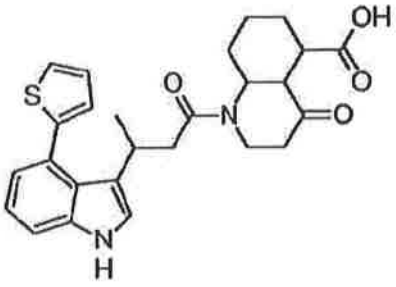

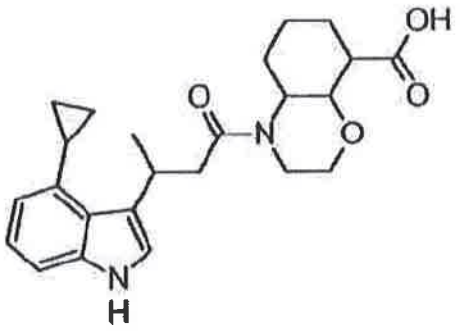
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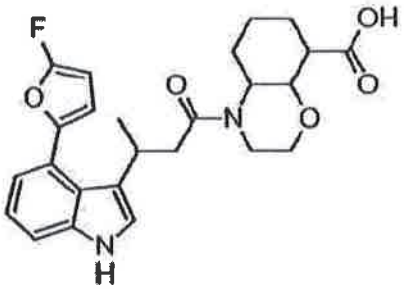
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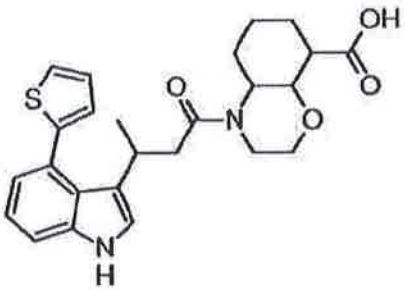
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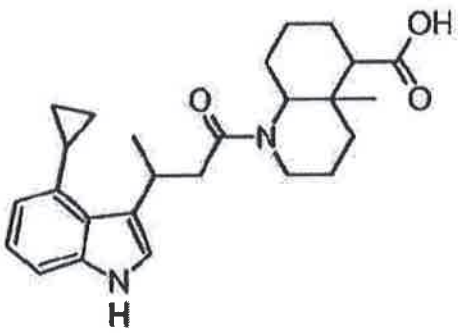
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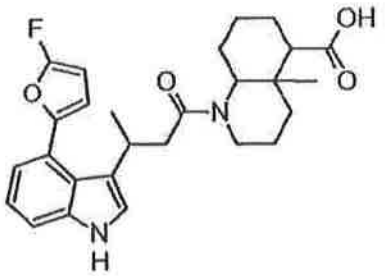

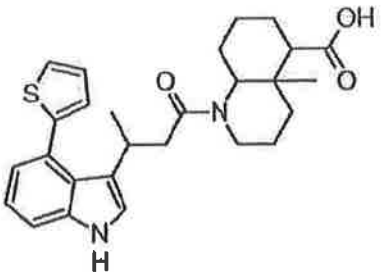

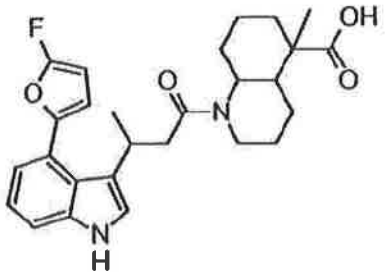

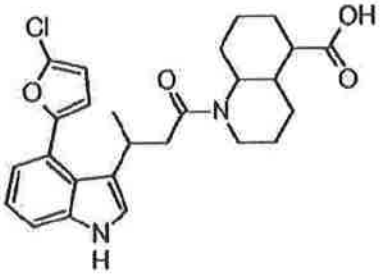

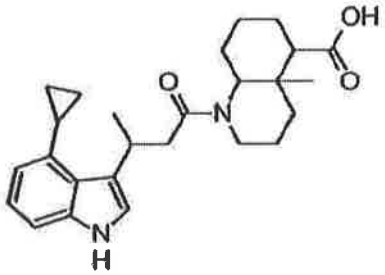

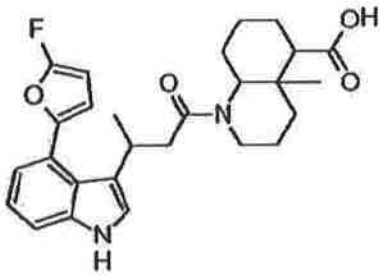

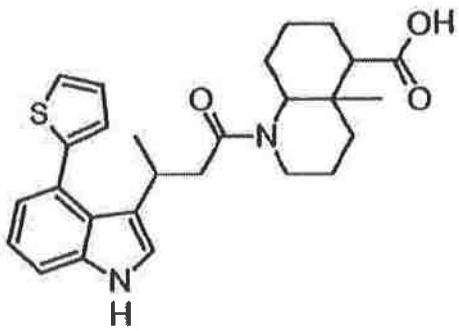

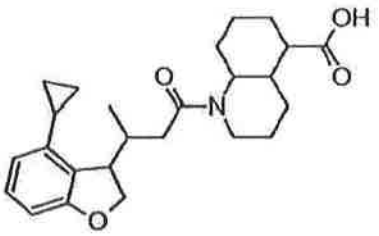

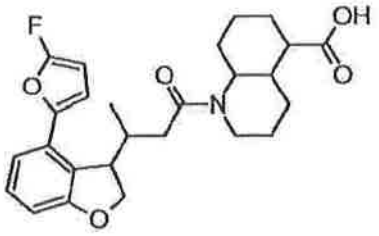

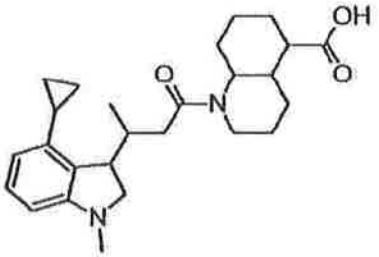

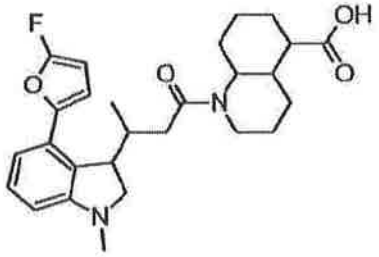

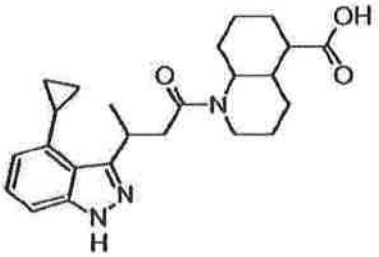

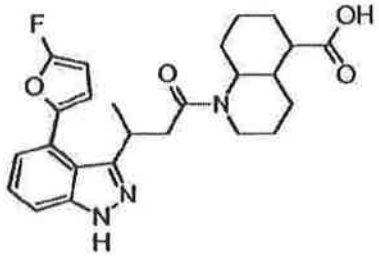

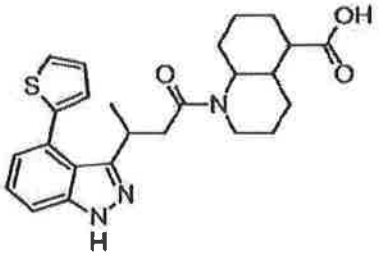

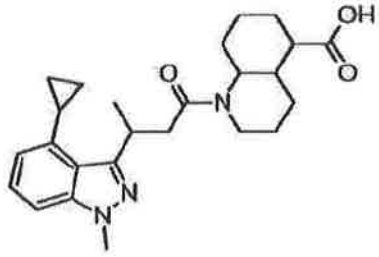

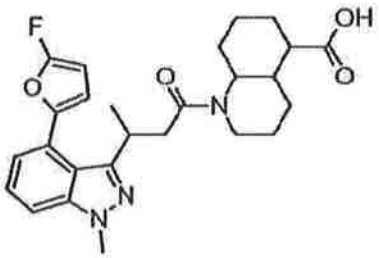

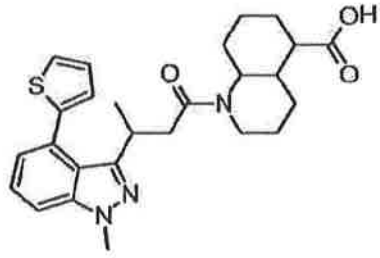

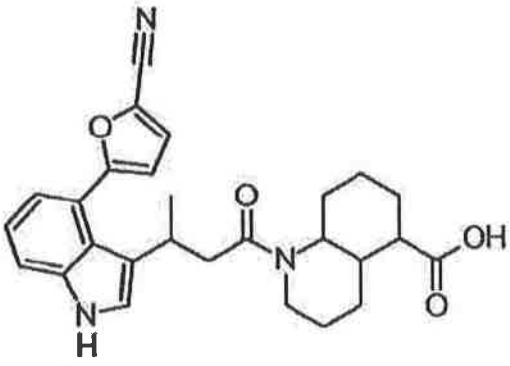

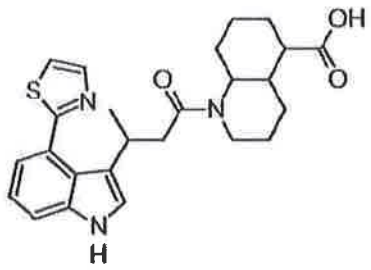

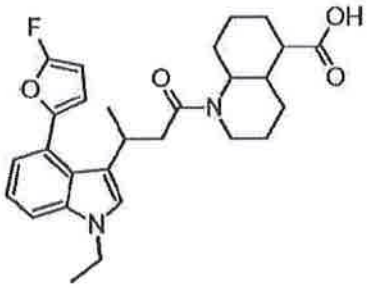

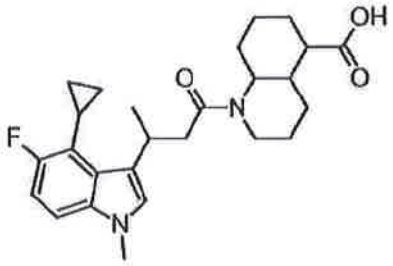

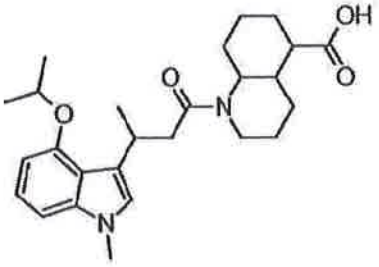

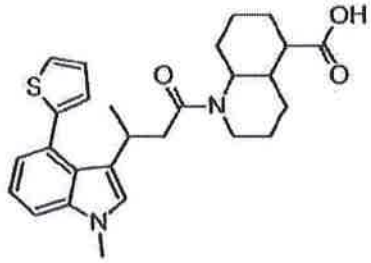

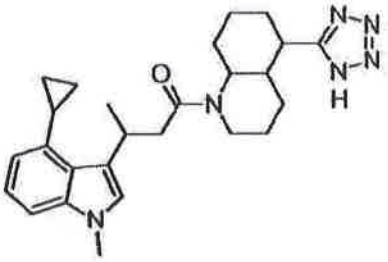

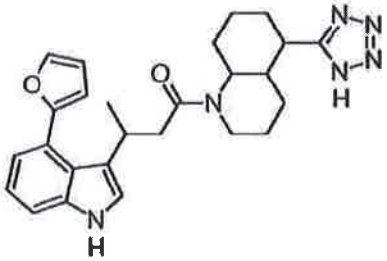

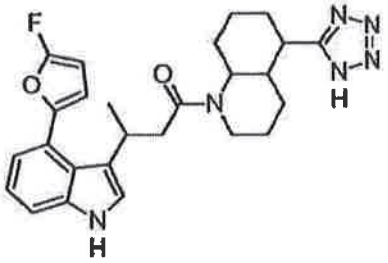

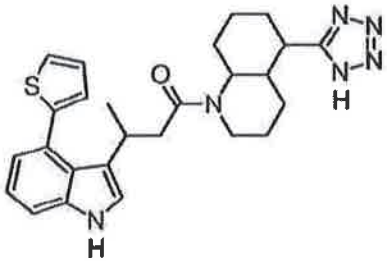

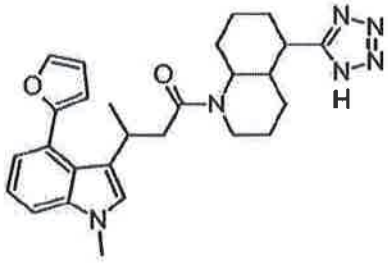

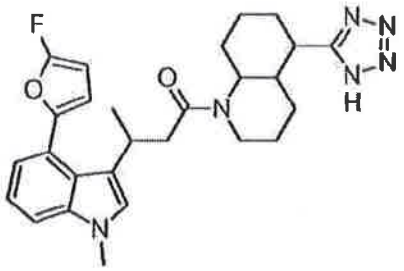

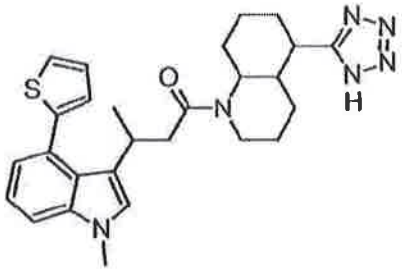

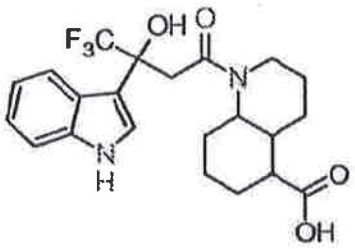

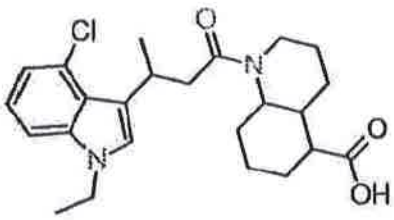

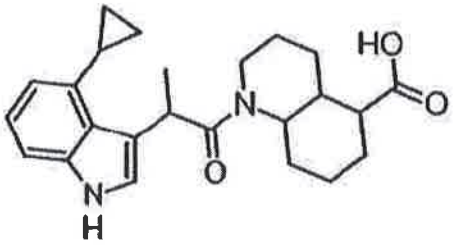

or pharmaceutically acceptable salt thereof.

7. A pharmaceutical composition including a compound according to claim 1 and a pharmaceutically acceptable diluent, excipient or carrier.

8. A method of treatment of a condition selected from

the group consisting of Type I diabetes, Type II diabetes, hyperglycemia, low glucose tolerance, hyperinsulinemia, hyperlipidemia, hypertriglyceridemia, hypercholesterolemia, dyslipidemia, obesity, abdominal obesity, glaucoma, hypertension, atherosclerosis and its sequelae, retinopathy, nephropathy, neuropathy, osteoporosis, osteoarthritis, dementia, depression, psychiatric disorders, Cushing's Disease, and Cushing's syndrome in a mammal, the method comprising administering an effective amount of a compound according to claim 1.

9. A method according to claim 8 wherein the condition is type II diabetes.

10. The method of claim 8, wherein the compound is administered in combination with an adjuvant.

11. The method of claim 10, wherein the adjuvant is selected from the group consisting of dipeptidyl peptidase-IV (DP-IV) inhibitors; (b) insulin sensitizing agents; (c) insulin and insulin mimetics; (d) sulfonylureas and other insulin secretagogues; (e) alpha-glucosidase inhibitors; (f) GLP-1, GLP-1 analogs, and GLP-1 receptor agonists; and combinations thereof.

12. The method of claim 11, wherein the insulin sensitizing agents are selected from the group consisting of (i) PPAR-gamma-agonists, (ii) PPAR-alpha-agonists, (iii) PPAR-alpha/gamma-dual agonists, (iv) biguanides, and combinations thereof.

13. A pharmaceutical composition including a compound according to claim 6 and a pharmaceutically acceptable diluent, excipient or carrier.

14. A method of treatment of a condition selected from the group consisting of Type I diabetes, Type II diabetes, hyperglycemia, low glucose tolerance, hyperinsulinemia, hyperlipidemia, hypertriglyceridemia, hypercholesterolemia, dyslipidemia, obesity, abdominal obesity, glaucoma, hypertension, atherosclerosis and its sequelae, retinopathy, nephropathy, neuropathy, osteoporosis, osteoarthritis, dementia, depression, psychiatric disorders, Cushing's Disease, and Cushing's syndrome, in a mammal, the method comprising administering an effective amount of a compound according to claim 6.

15. A method according to claim 6 wherein the condition is type II diabetes.

16. The method of claim 6, wherein the compound is administered in combination with an adjuvant.

17. The method of claim 6, wherein the adjuvant is selected from the group consisting of dipeptidyl peptidase-IV (DP-IV) inhibitors; (b) insulin sensitizing agents; (c) insulin and insulin mimetics; (d) sulfonylureas and other insulin secretagogues; (e) alpha-glucosidase inhibitors; (f) GLP-1, GLP-1 analogs, and GLP-1 receptor agonists; and combinations thereof.

18. The method of claim 6, wherein the insulin sensitizing agents are selected from the group consisting of (i) PPAR-gamma-agonists, (ii) PPAR-alpha-agonists, (iii) PPAR-alpha/gamma-dual agonists, (iv) biguanides, and combinations thereof.

CLEAN COPY - AMENDMENTS UNDER ART. 34

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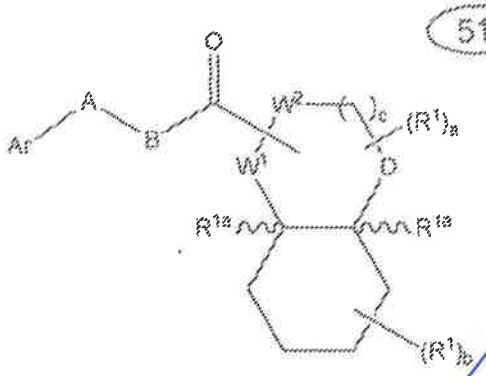
(51)

Claims:

1. A compound of formula (I):



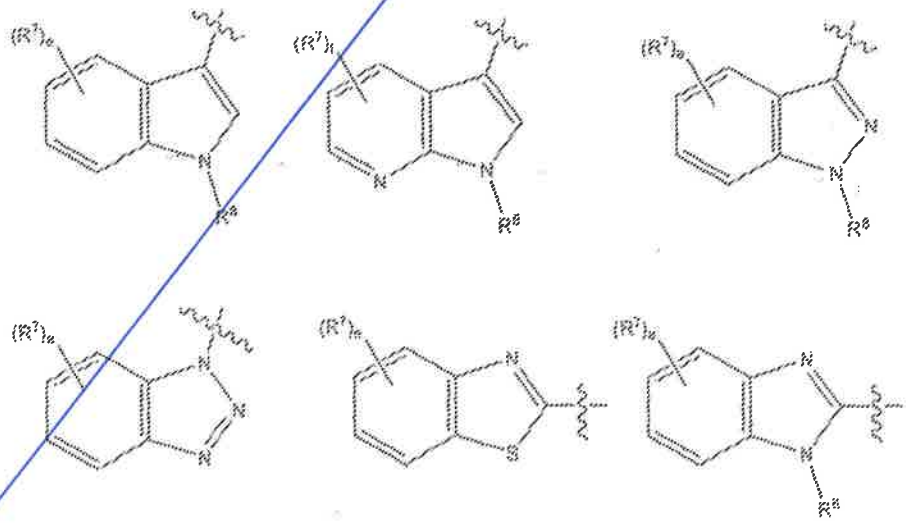
Formula (I)

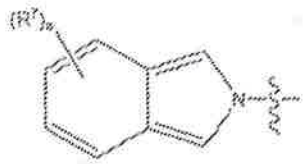
wherein:

each R^1 and R^{1a} is independently selected from the group consisting of H, methyl, $CONHC(CH_3)_3$, OH, CO_2H, CO_2CH_3, $CO_2CH_2CH_3$, phenyl, CH_2OH, CN and OCH_3.

or any two R^1 on adjacent carbon atoms may be joined to form a cyclic moiety, or any two R^1 on the same carbon when taken together may form a group of the formula =O

Ar is an optionally substituted C_1-C_9heteroaryl group selected from the group consisting of:



and 

wherein each R^7 is independently selected from the group consisting of H, halogen, OH, NO_2, CN, SH, NH_2, CF_3, OCF_3, optionally substituted C_1-C_{12}alkyl, optionally substituted C_1-C_{12}haloalkyl, optionally substituted C_2-C_{12}alkenyl, optionally substituted C_2-C_{12}alkynyl, optionally substituted C_2-C_{12}heteroalkyl, optionally substituted C_3-C_{12}cycloalkyl, optionally substituted C_3-C_{12}cycloalkenyl, optionally substituted C_2-C_{12}heterocycloalkyl, optionally substituted C_2-C_{12}heterocycloalkenyl, optionally substituted C_6-C_{18}aryl, optionally substituted C_1-C_{18}heteroaryl, optionally substituted C_1-C_{12}alkyloxy, optionally substituted C_2-C_{12}alkenyloxy, optionally substituted C_2-C_{12}alkynyloxy, optionally substituted C_3-C_{12}heteroalkyloxy, optionally substituted C_3-C_{12}cycloalkyloxy, optionally substituted C_3-C_{12}cycloalkenyloxy, optionally substituted C_2-C_{12}heterocycloalkyloxy, optionally substituted C_2-C_{12} heterocycloalkenyloxy, optionally substituted C_6-C_{18}aryloxy, optionally substituted C_1-C_1 heteroaryloxy, optionally substituted C_1-C_{12}alkylamino, SR^9, SO_3H, $SO_2NR^9R^{10}$, SO_2R^9, $SONR^9R^{10}$, SOR^9, COR^9, COOH, $COOR^9$, $CONR^9R^{10}$, NR^9COR^{10}, NR^9COOR^{10}, $NR^9SO_2R^{10}$, $NR^9CONR^9R^{10}$, NR^9R^{10}, and acyl;

wherein R^8 is selected from the group consisting of H, optionally substituted C_1-C_{12}alkyl, optionally substituted C_2-C_{12}alkenyl, optionally substituted C_2-C_{12}alkynyl, optionally substituted C_2-C_{12}heteroalkyl, optionally substituted C_3-C_{12}cycloalkyl, optionally substituted C_2-C_{12}heterocycloalkyl, optionally substituted C_6-C_{18}aryl, optionally substituted C_1-C_{18}heteroaryl, SO_3H, $SO_2NR^9R^{10}$, SO_2R^9, $SONR^9R^{10}$, SOR^9, COR^9, COOH, $COOR^9$, and $CONR^9R^{10}$;

wherein each R^9 and R^{10} is independently selected from the group consisting of H, optionally substituted C_1-C_{12}alkyl, optionally substituted C_2-C_{10}heteroalkyl, optionally substituted C_1-C_{12}haloalkyl, optionally substituted C_3-C_{12}cycloalkyl, optionally substituted C_6-C_{18}aryl, and optionally substituted C_1-C_{18}heteroaryl.

e is an integer selected from the group consisting of 0, 1, 2, 3 and 4;

f is an integer selected the group consisting of 0, 1, 2, and 3;

A is $-CR^aR^b-$;

B is a group of the formula $-(CR^cR^d)_n-$;

wherein each R^a, R^b, R^c and R^d is independently selected from the group consisting of H, halogen, OH, NO_2, CN, SH, NH_2, CF_3, OCF_3, C_1-C_{12}alkyl, C_2-C_{10}heteroalkyl, C_1-C_{12}haloalkyl, C_3-C_{12}cycloalkyl, C_6-C_{18}aryl, C_1-C_{18}heteroaryl; SR^2, SO_3H, $SO_2NR^2R^3$, SO_2R^2, $SONR^2R^3$, SOR^2, COR^2, COOH, $COOR^2$, $CONR^2R^3$, NR^2COR^3, NR^2COOR^3, $NR^2SO_2R^3$, $NR^2CONR^2R^2$, NR^2R^3, and acyl,

wherein each R^2 and R^3 is independently selected from the group consisting of H, C_1-C_{12}alkyl, C_2-C_{10}heteroalkyl, C_1-C_{12}haloalkyl, C_3-C_{12}cycloalkyl, C_6-C_{18}aryl, and C_1-C_{18}heteroaryl;

W^1 and W^2 are selected such that one is N and the other is $(CR^1{}_2)$,

the bond from the carbonyl carbon is joined to whichever of W^1 or W^2 is N,

D is O or $(CR^1{}_2)$,

n is an integer selected from the group consisting of 0, 1, and 2;

a is an integer selected from the group consisting of 0, 1, and 2, 3 ;

b is an integer selected from the group consisting of 0, 1, 2, 3, 4, 5, 6, 7, and 8,

c is 1;

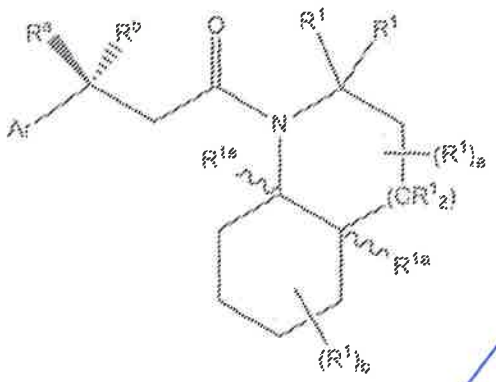
or a pharmaceutically acceptable salt thereof.

2. A compound according to claim 1 wherein D is $(CR^1{}_2)$.

3. A compound according to claim 1 or 3 wherein B is CH_2.

4. A compound according to any one of claims 1 to 3 wherein R^a and R^b are different.

5. A compound according to claim 1 having the formula:



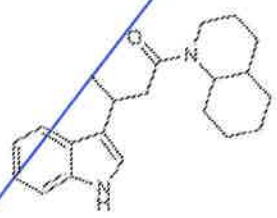
wherein Ar, R^a, R^b, R^1, R^{1a}, a and b are as defined in claim 1.

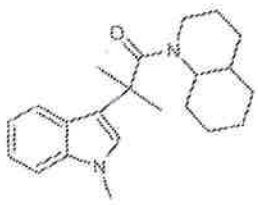
6. A compound according to claim 5 wherein one of R^a and R^b is H and the other is optionally substituted alkyl.

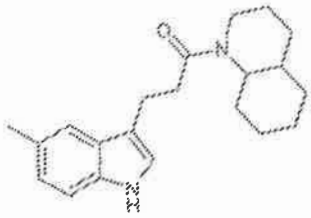
7. A compound according to claim 1 wherein the R^7 substituent is located in the 4 or the 5 position of the six membered ring.

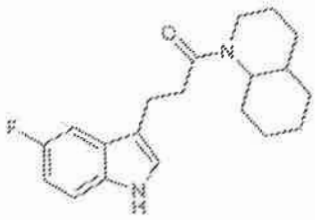
8. A compound according to claim 1 wherein R^7 is selected from the group consisting of CH_3, CH_2CH_3, $CH_2CH_2CH_3$, $CH(CH_3)_2$, $(CH_2)_3CH_3$ Cl, Br, F, I, OH, NO_2, NH_2, CN, SO_3H, OCH_3, $OCH_2CH_2CH_3$, CF_3, and OCF_3.

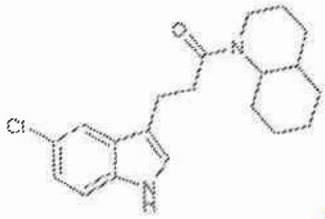
9. A compound according to claim 1 selected from the group consisting of:

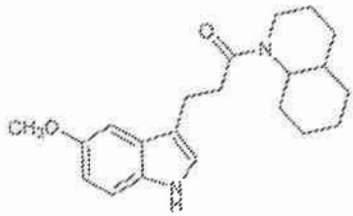


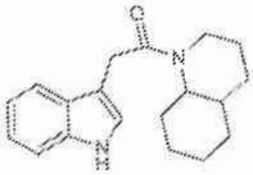


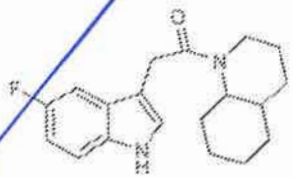


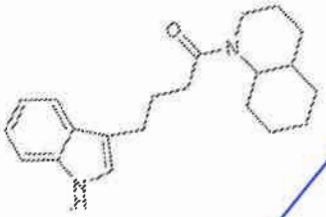


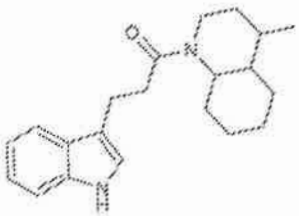


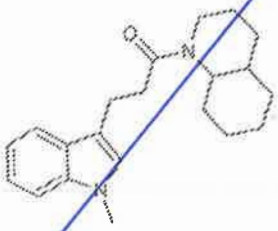


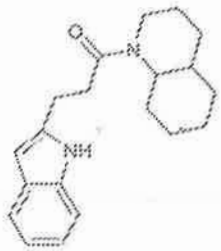


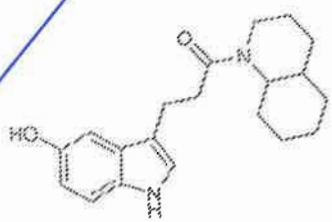


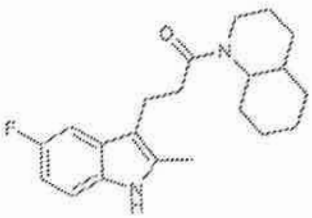


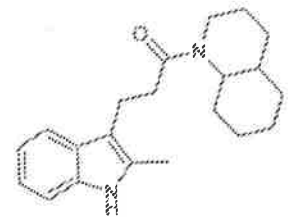


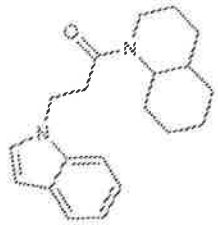


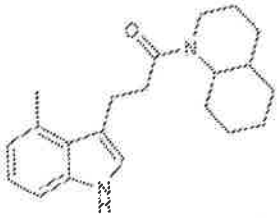


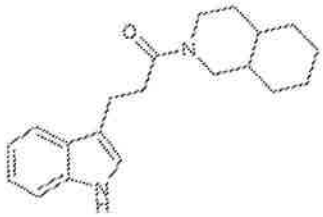


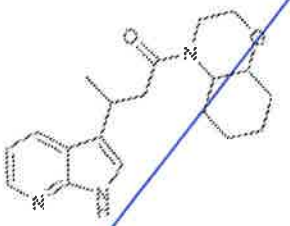


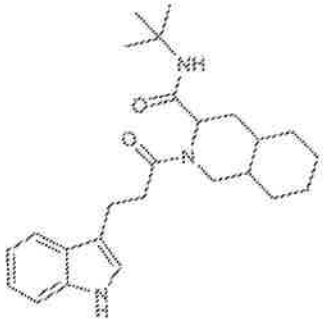


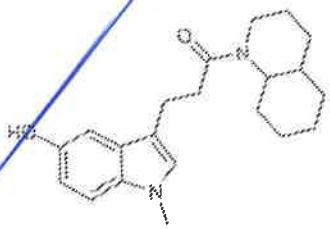


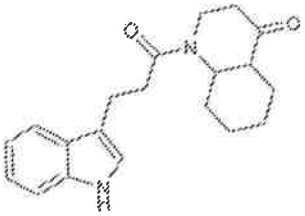


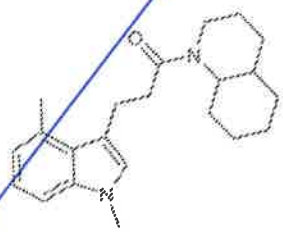


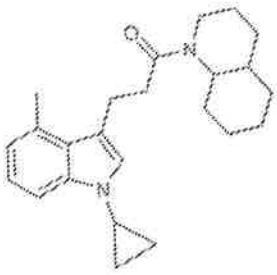


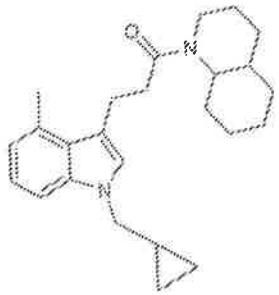


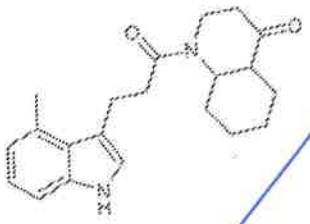


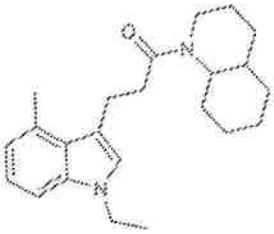


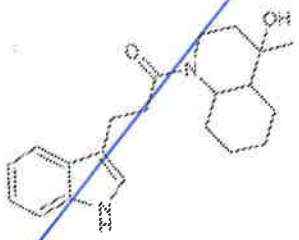


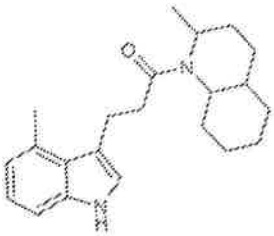


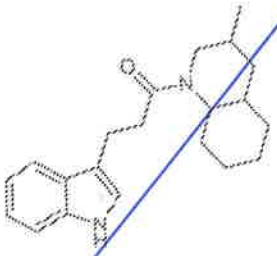


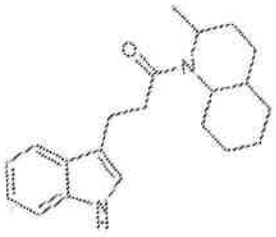


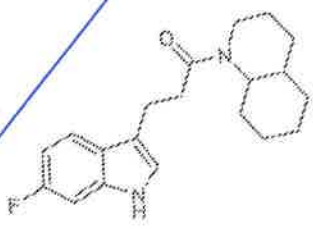


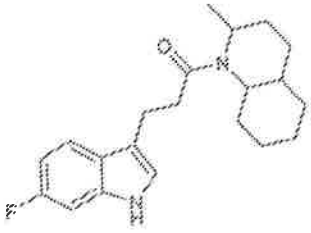


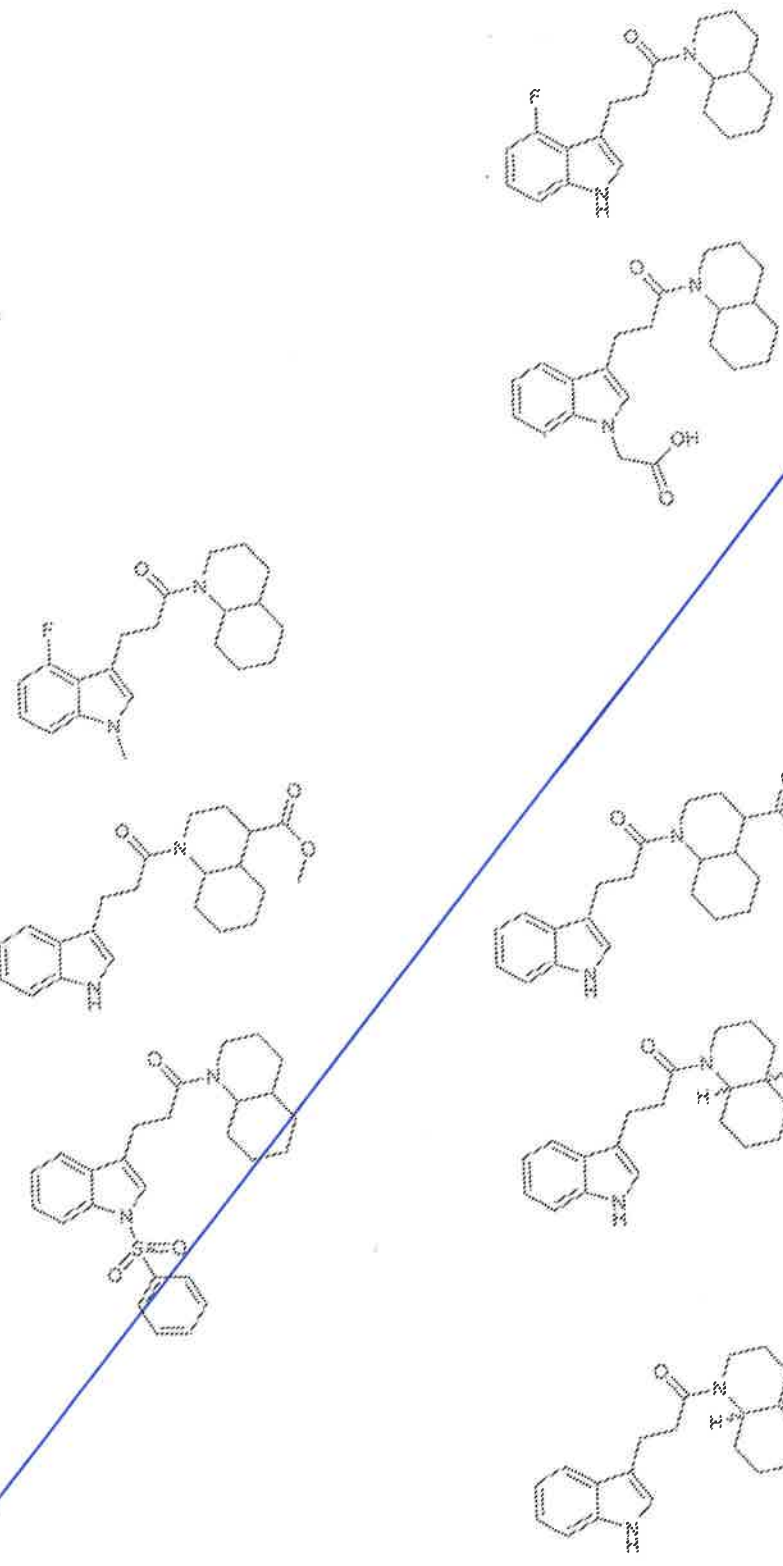


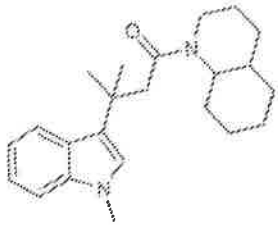


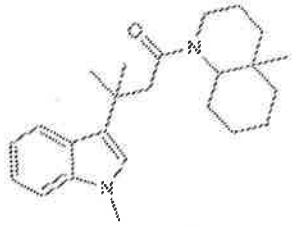


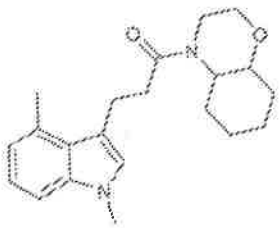


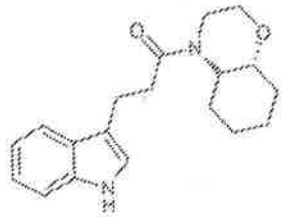


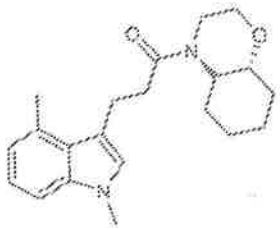


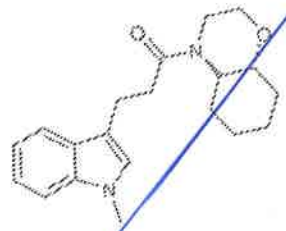


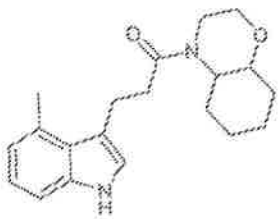


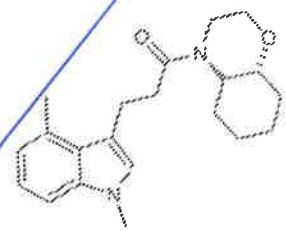


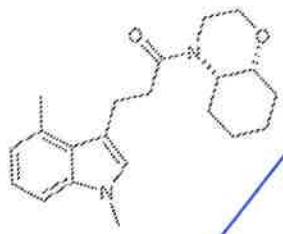


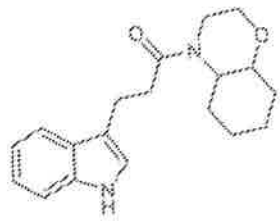


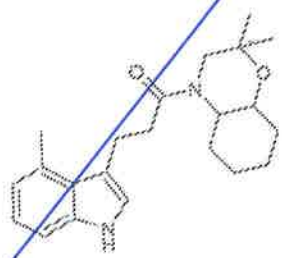


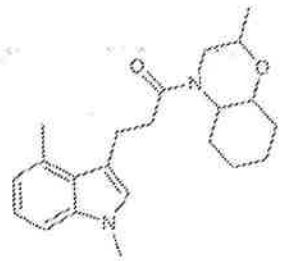


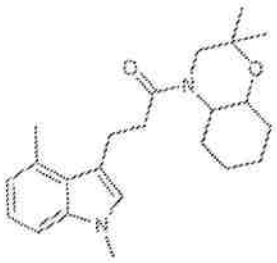


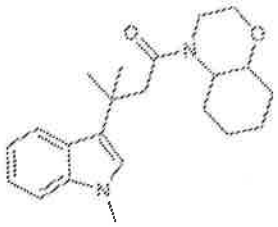


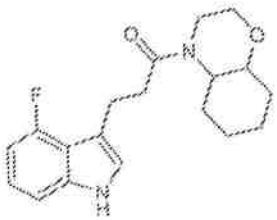


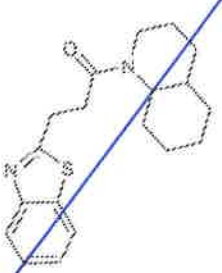


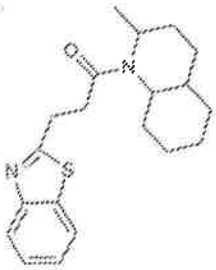


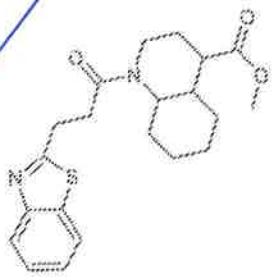


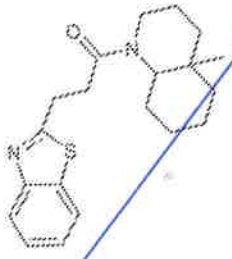


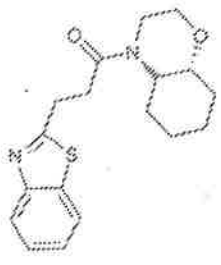


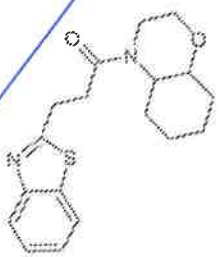


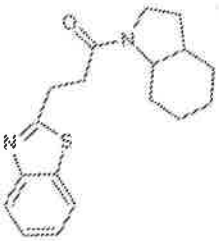


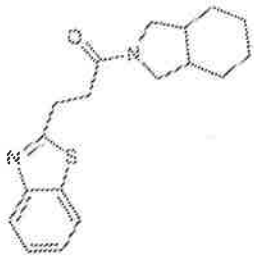


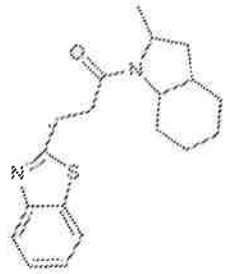


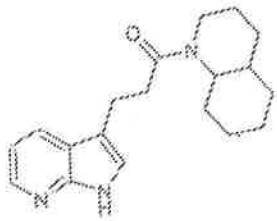


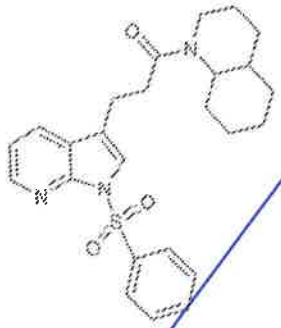


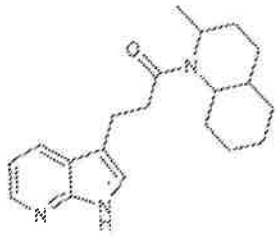


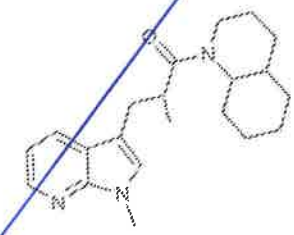


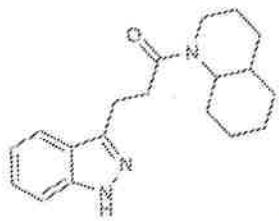


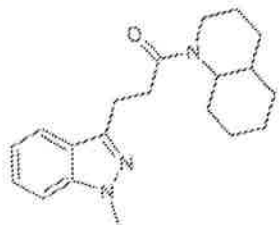


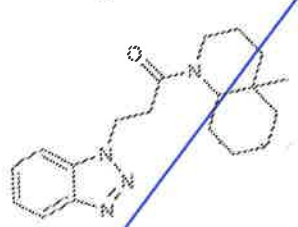


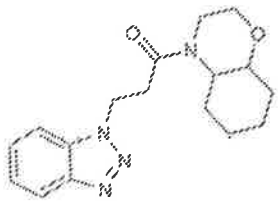


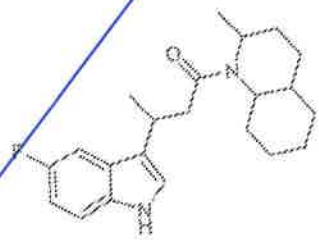


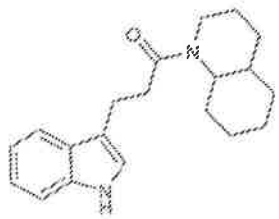


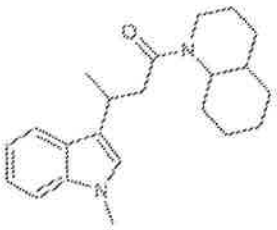


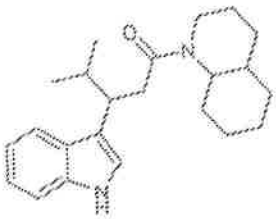


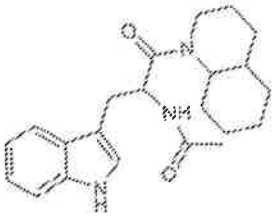


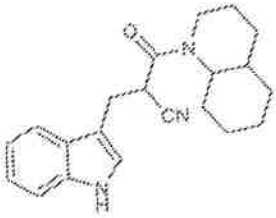


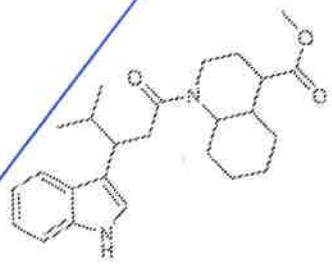


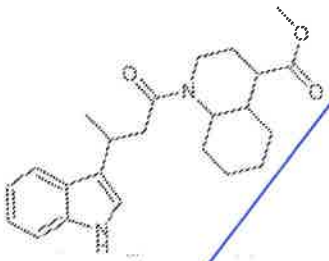


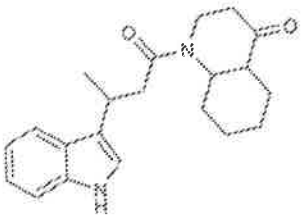


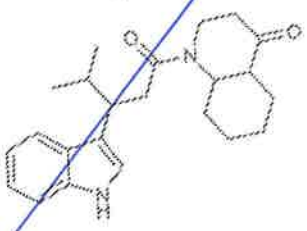


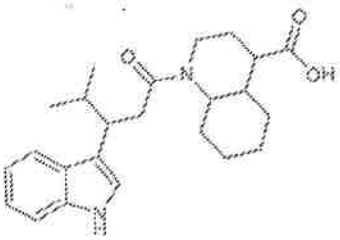


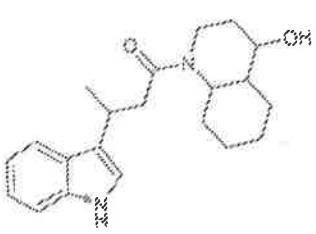


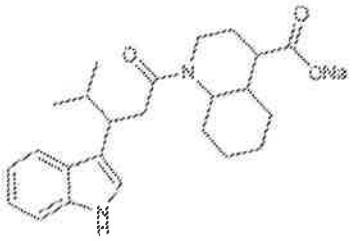


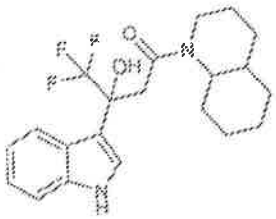


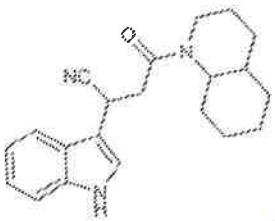


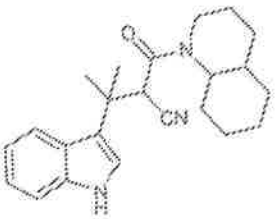


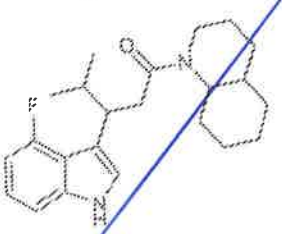


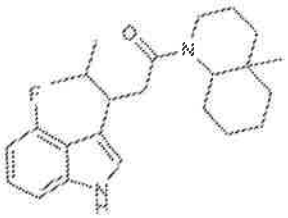


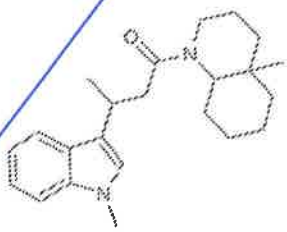


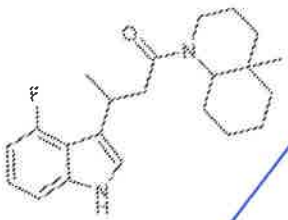


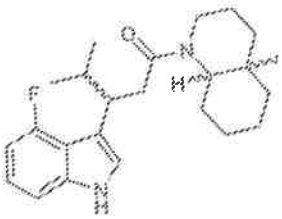


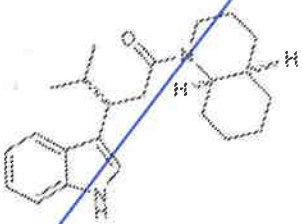


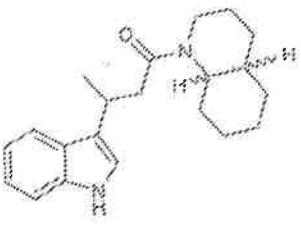


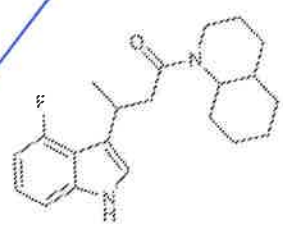


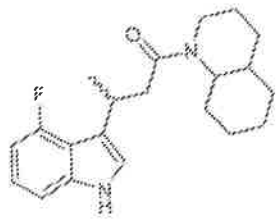


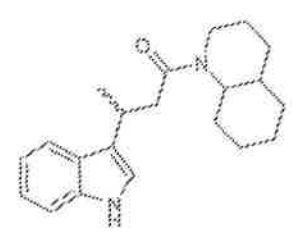
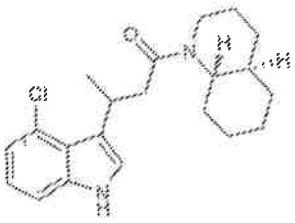
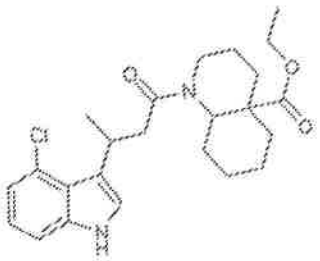
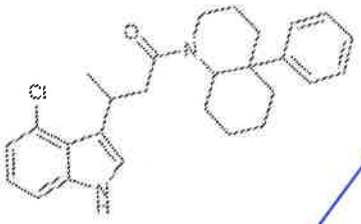
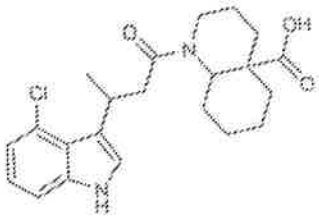
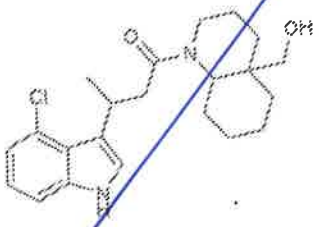
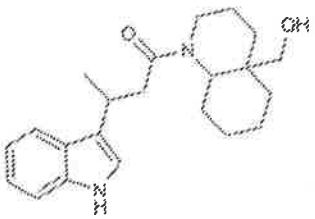
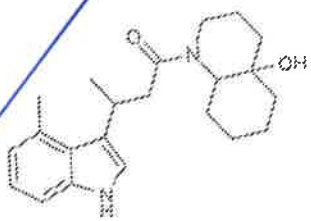
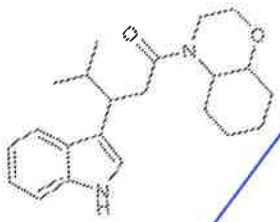
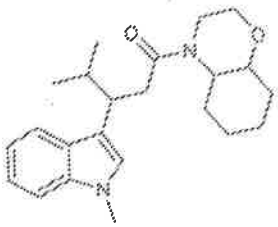
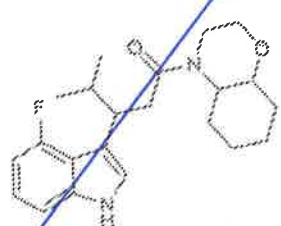
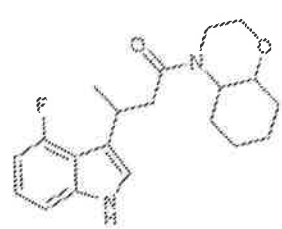
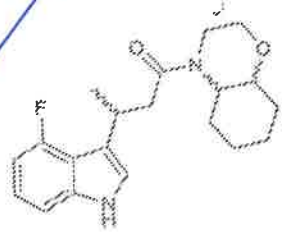
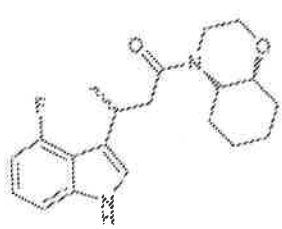


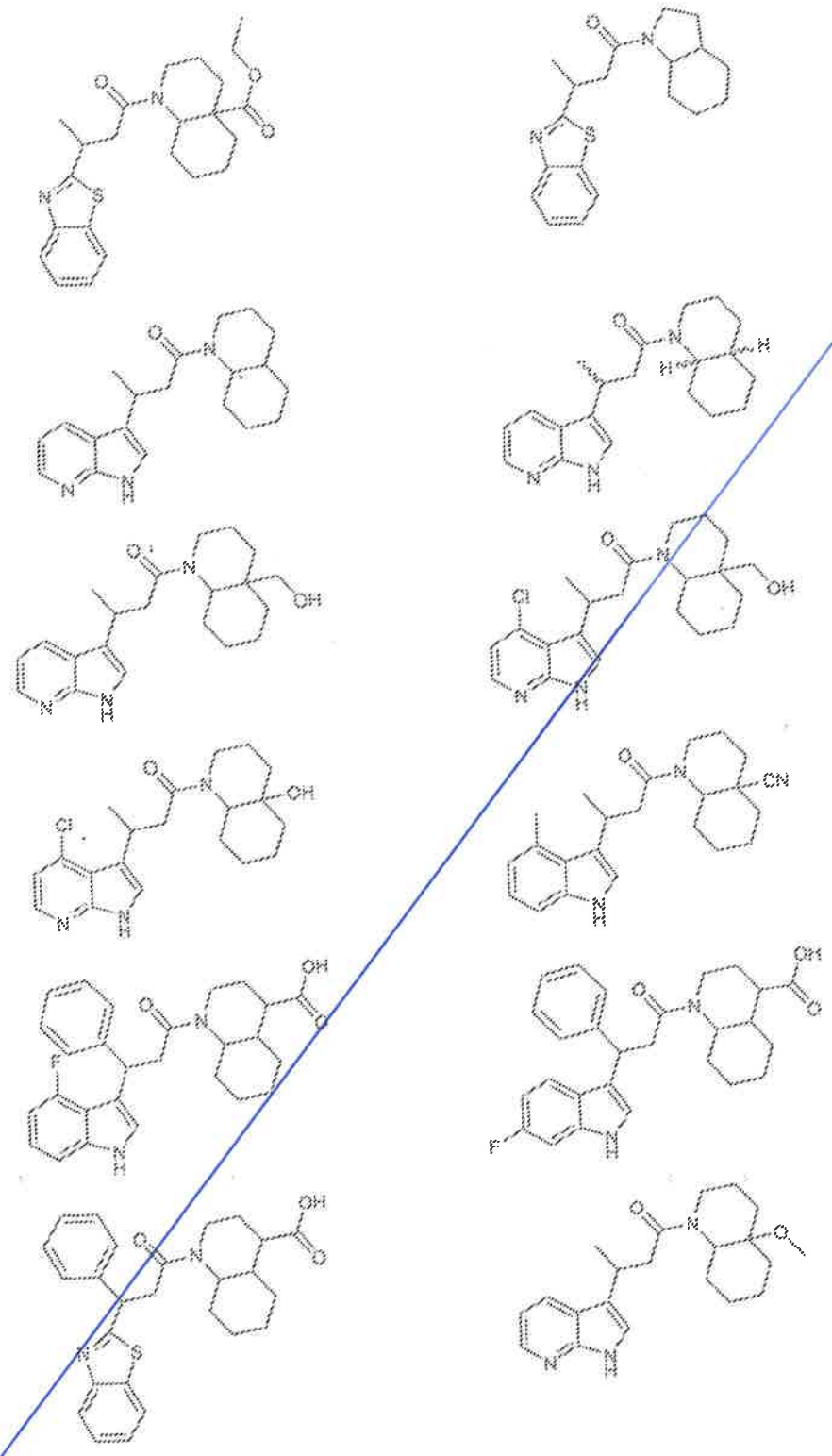


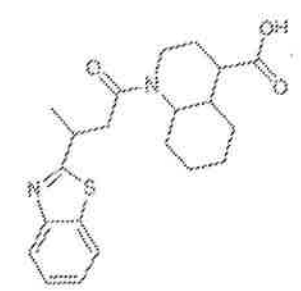
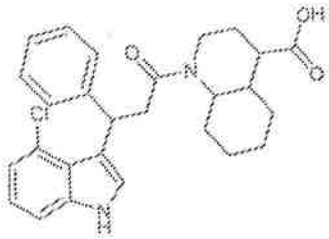
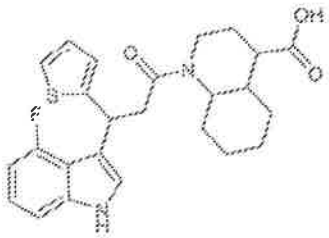
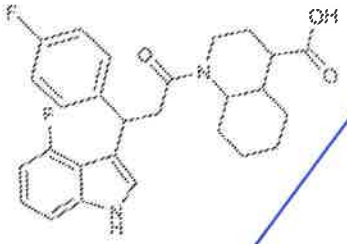
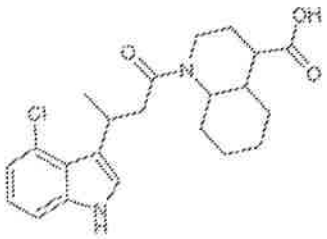
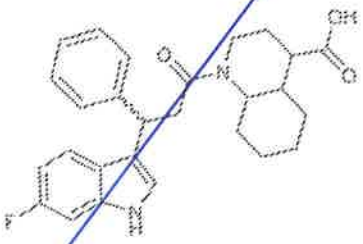
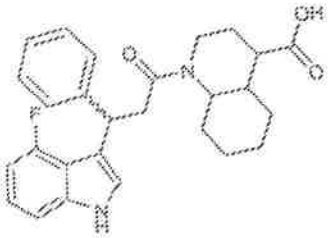
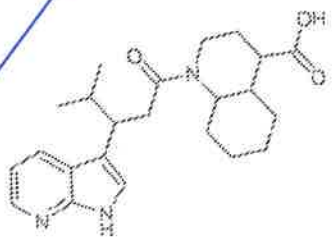
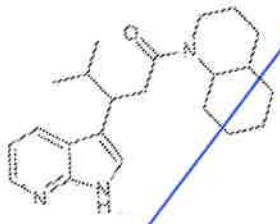
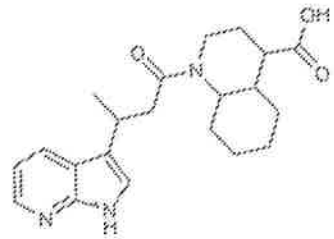
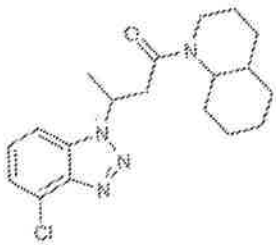


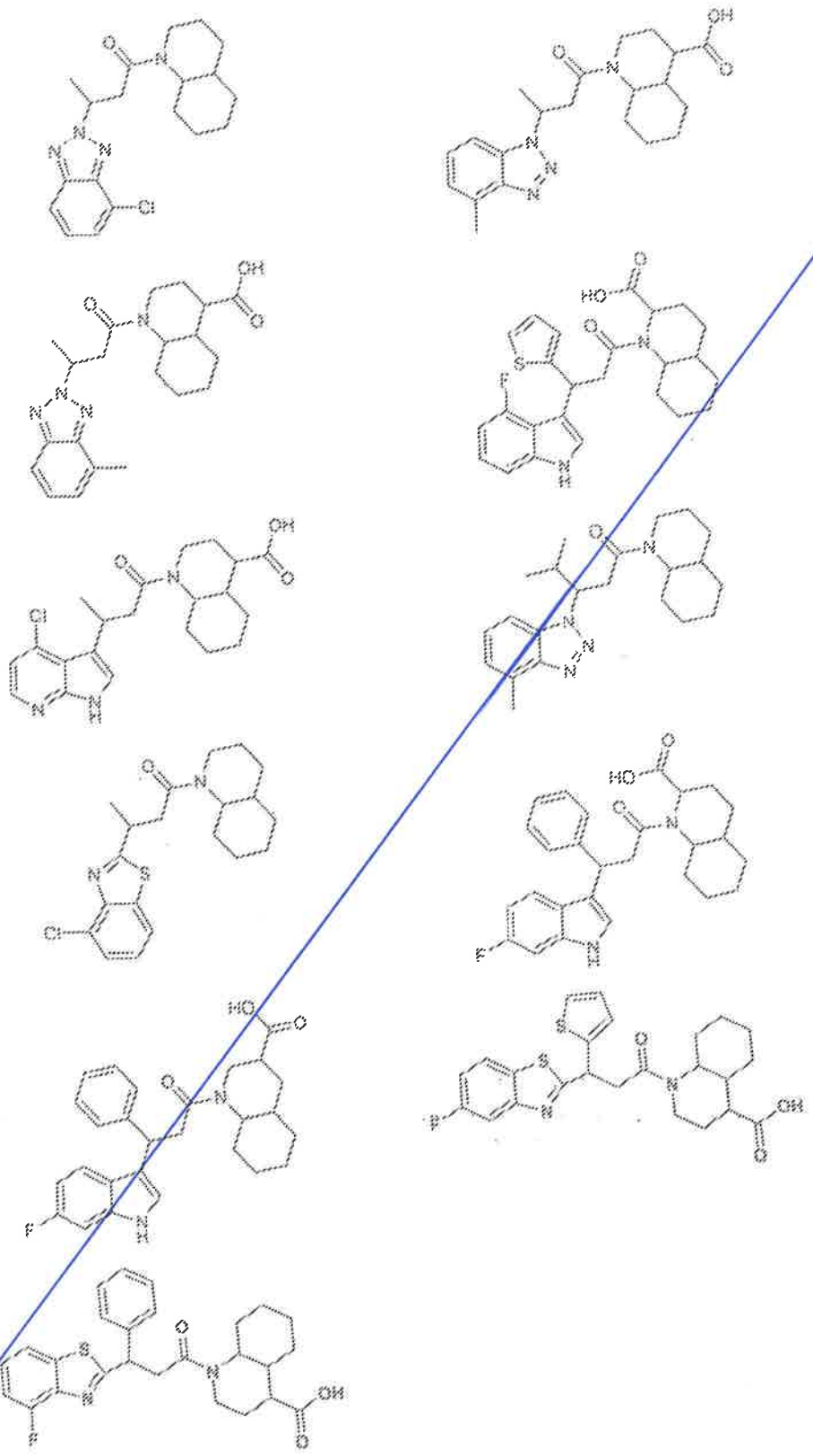


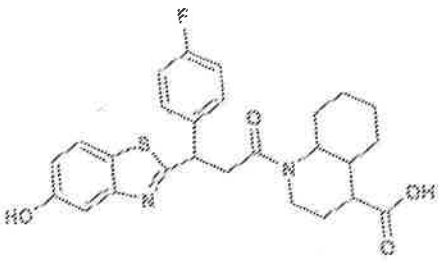
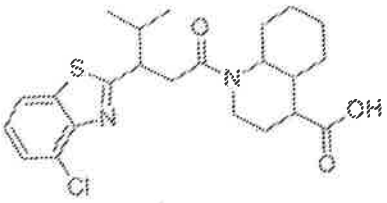
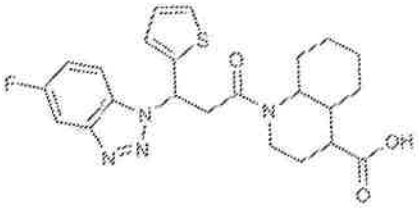
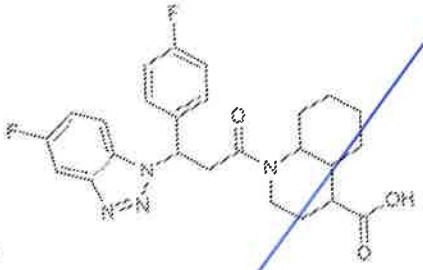
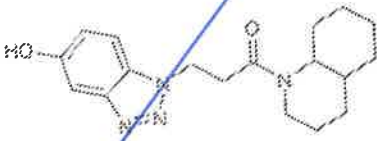
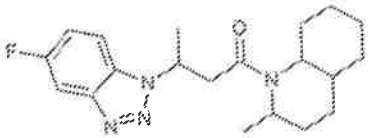
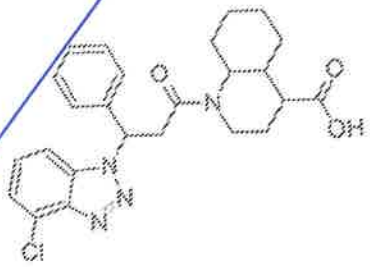
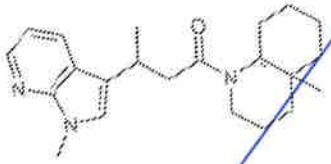
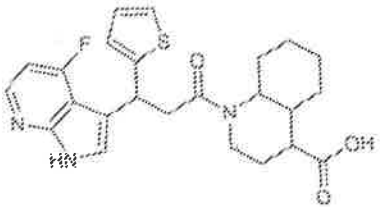
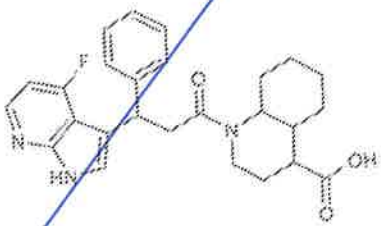
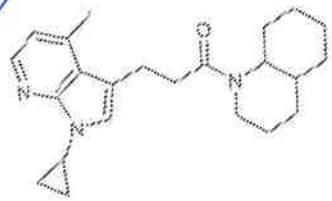
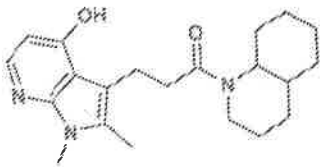


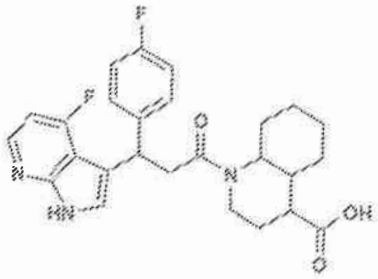
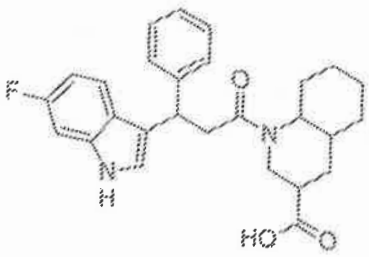
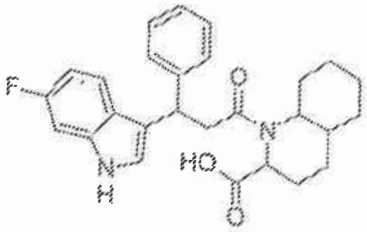
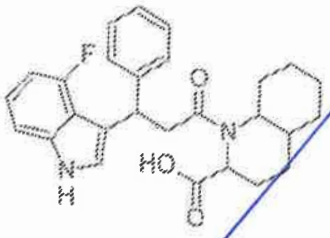
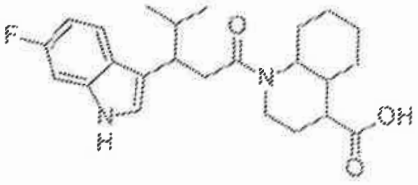
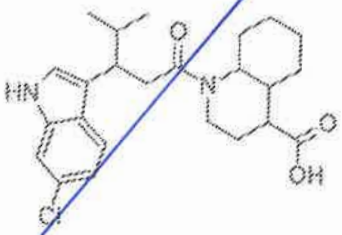
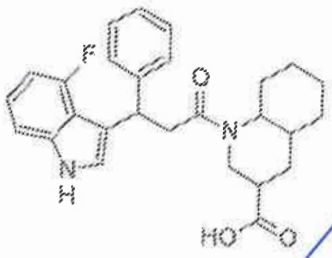
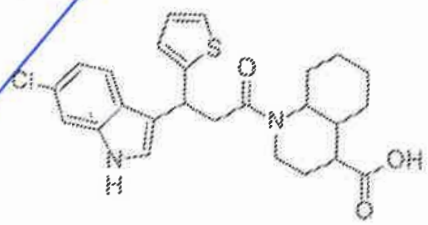
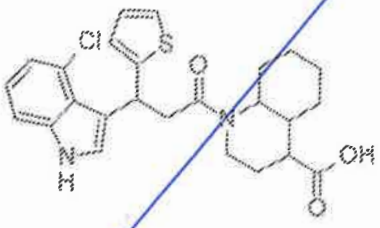
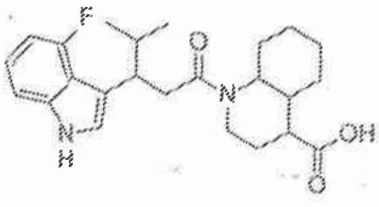
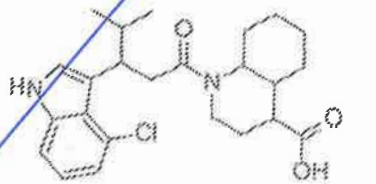
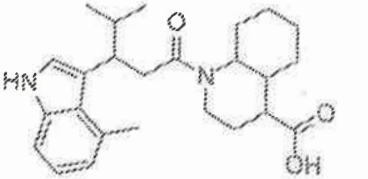

















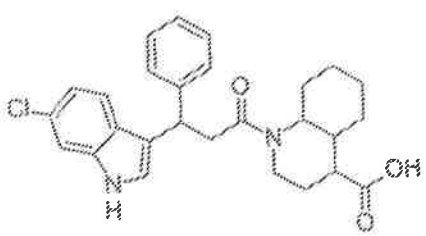
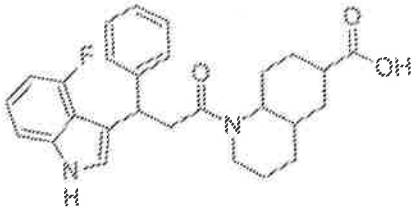
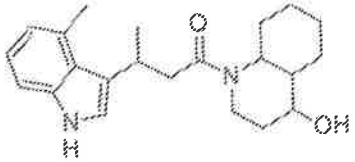
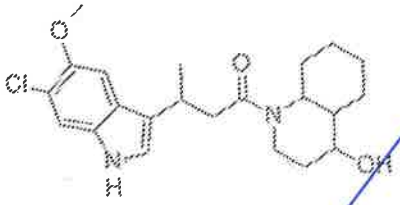
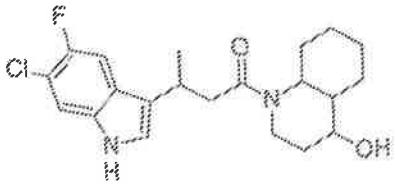
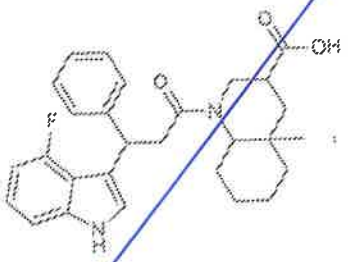
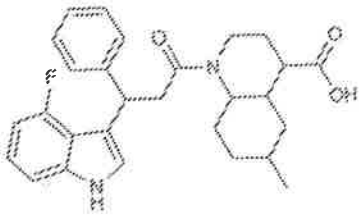
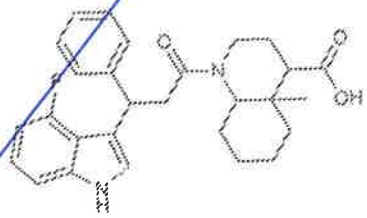
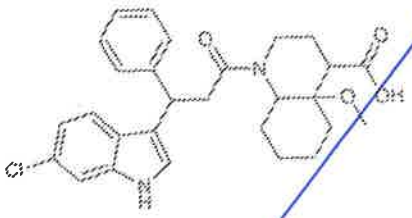
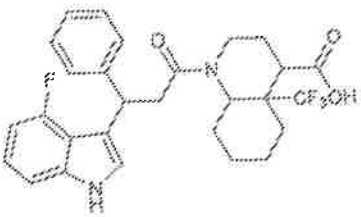
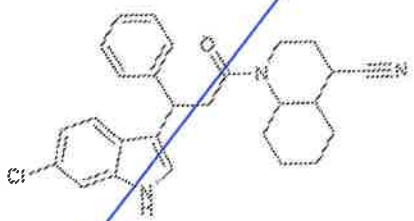
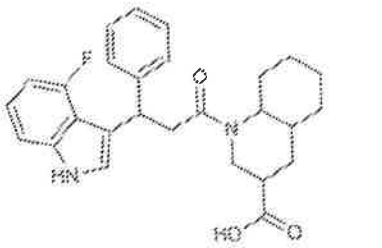
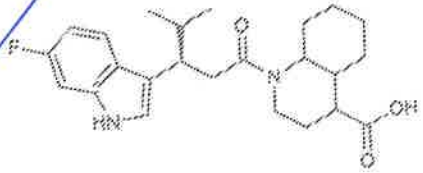
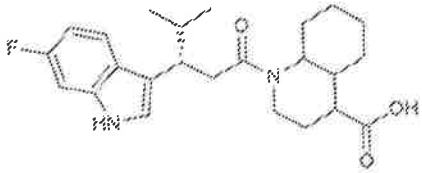












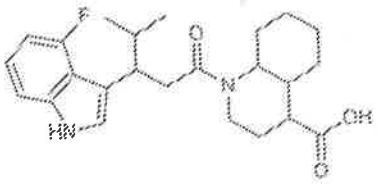
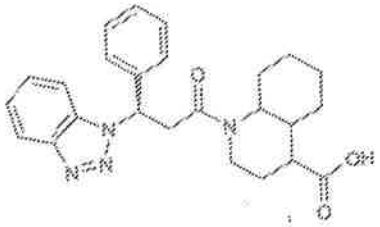
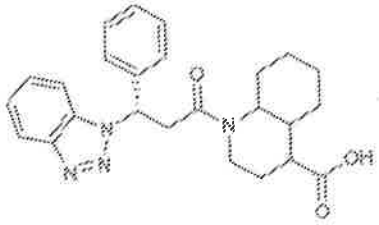
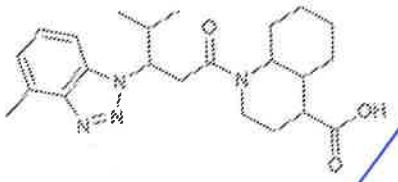
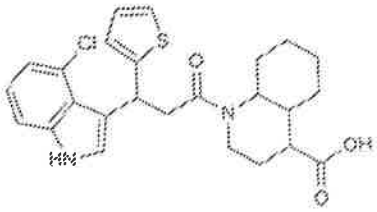
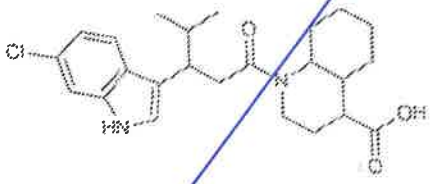
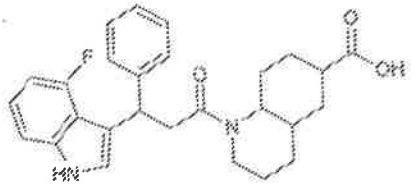
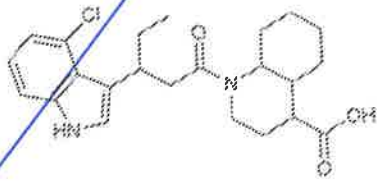
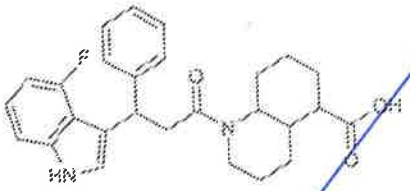
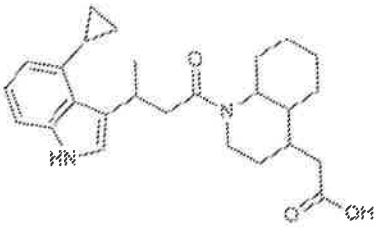
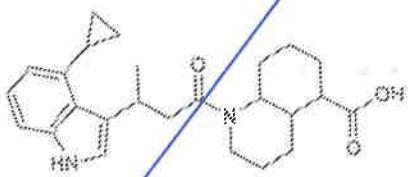
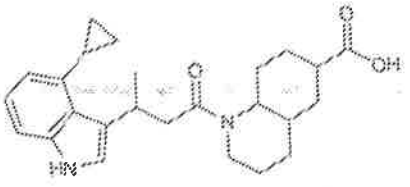
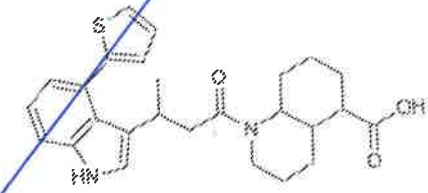
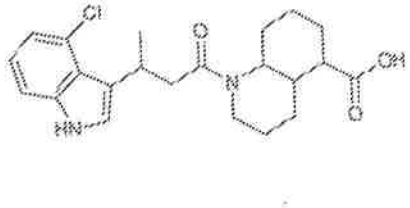


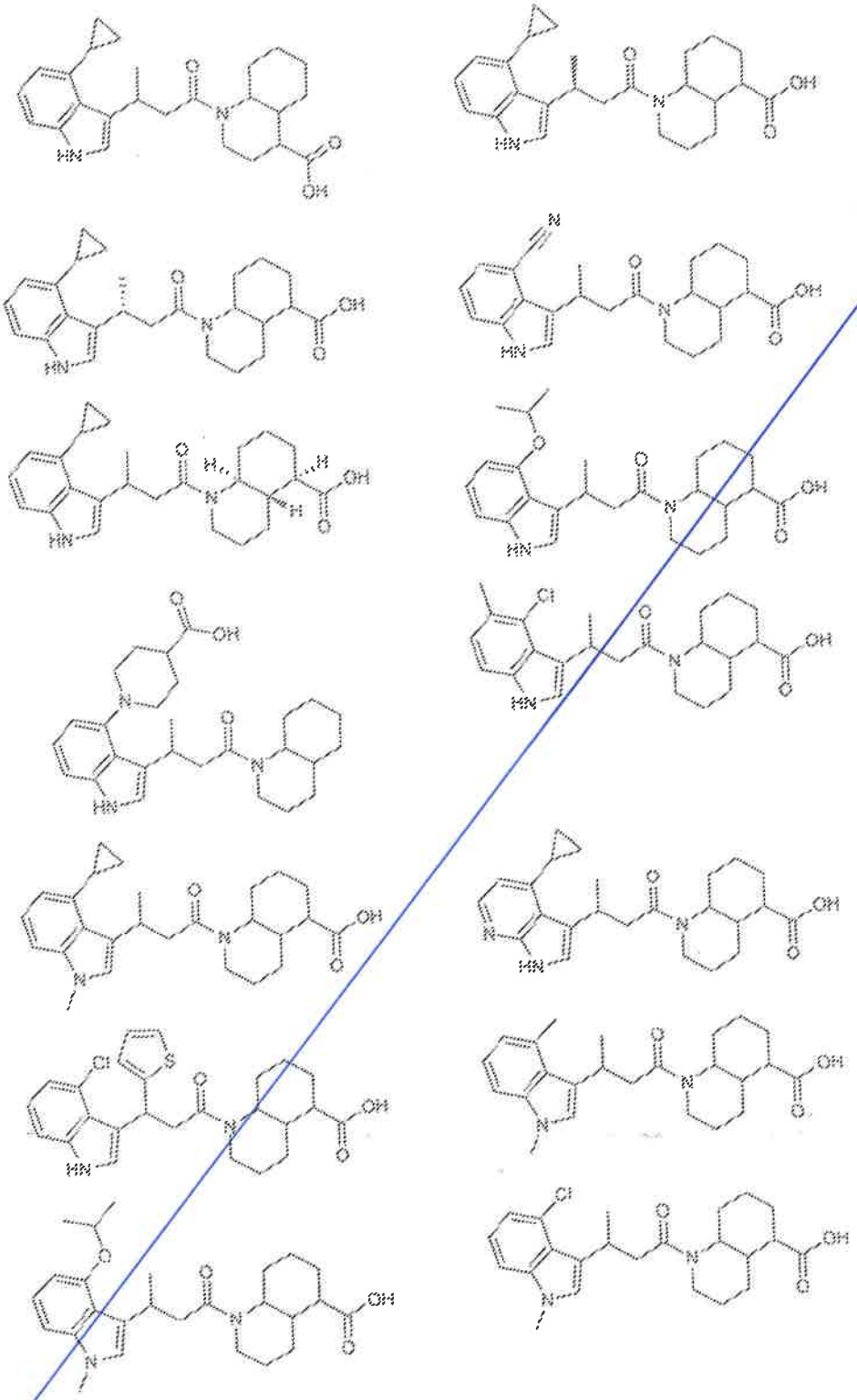













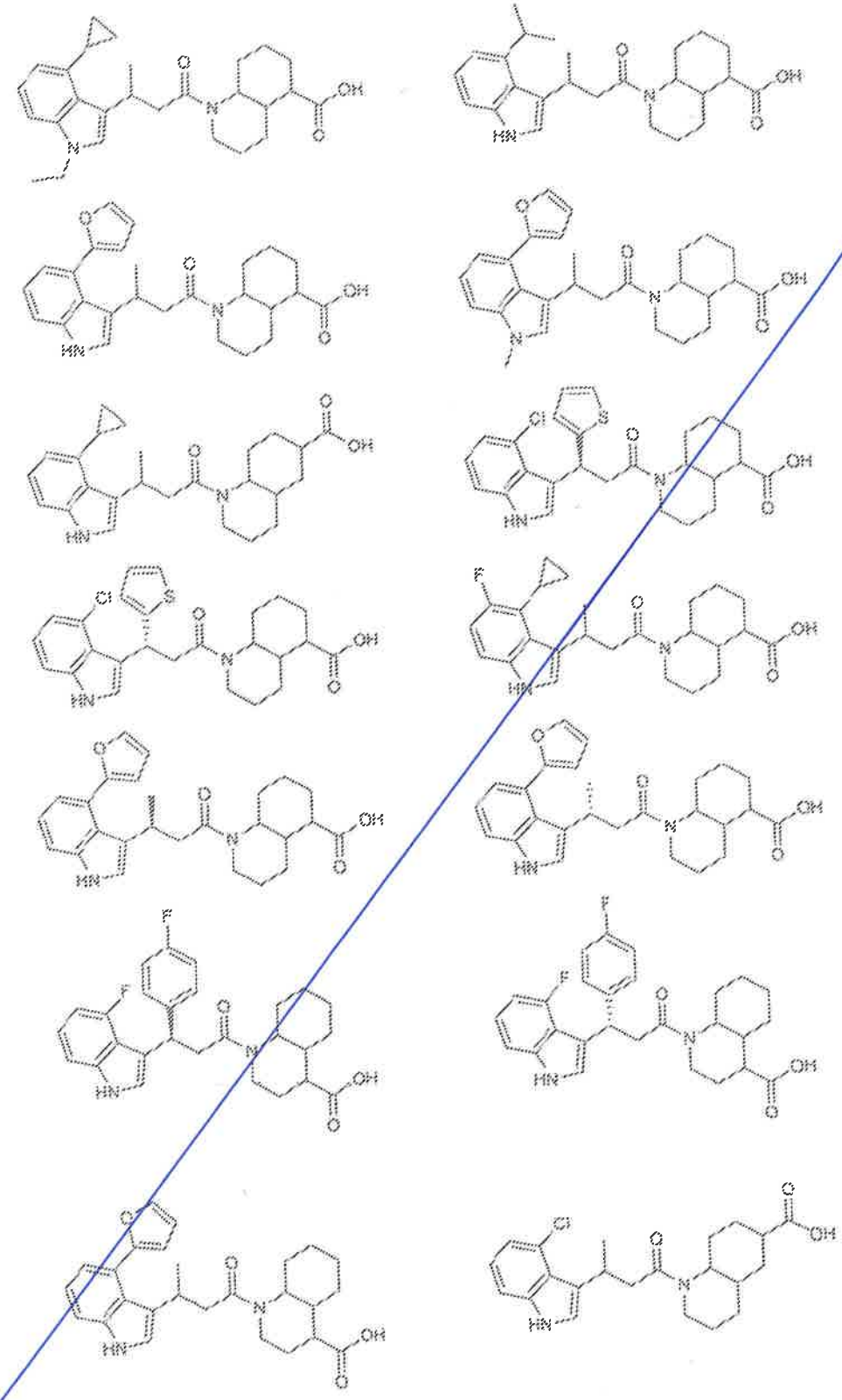













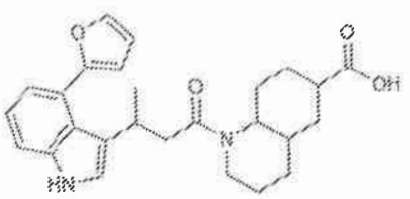
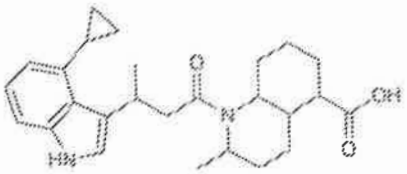
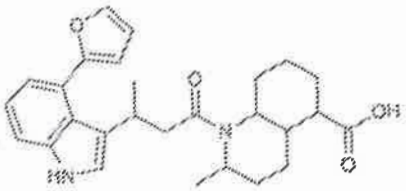
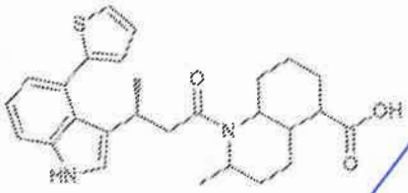
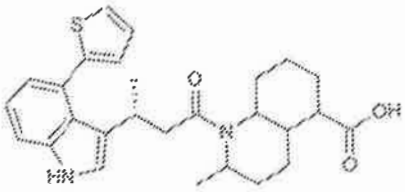
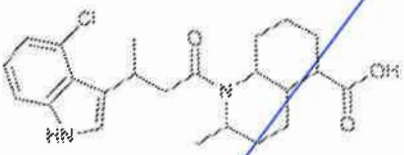
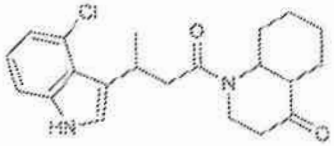
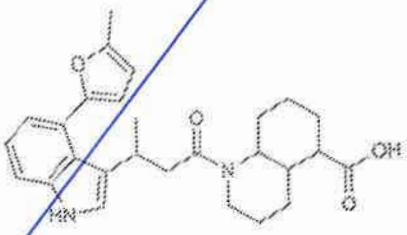
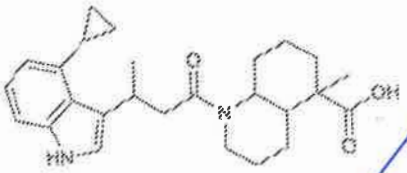
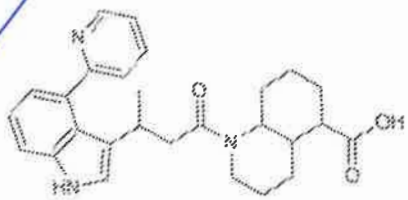
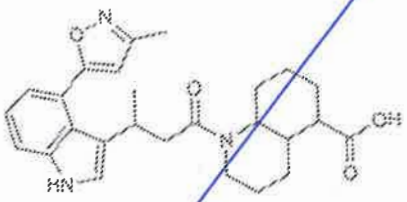
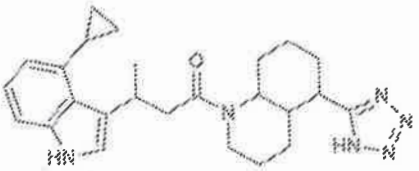
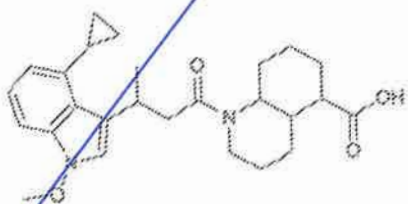
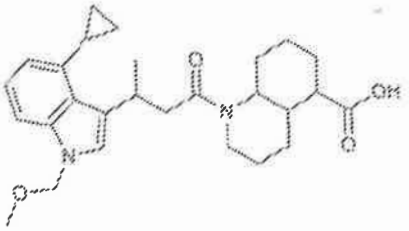
AMENDED SHEET

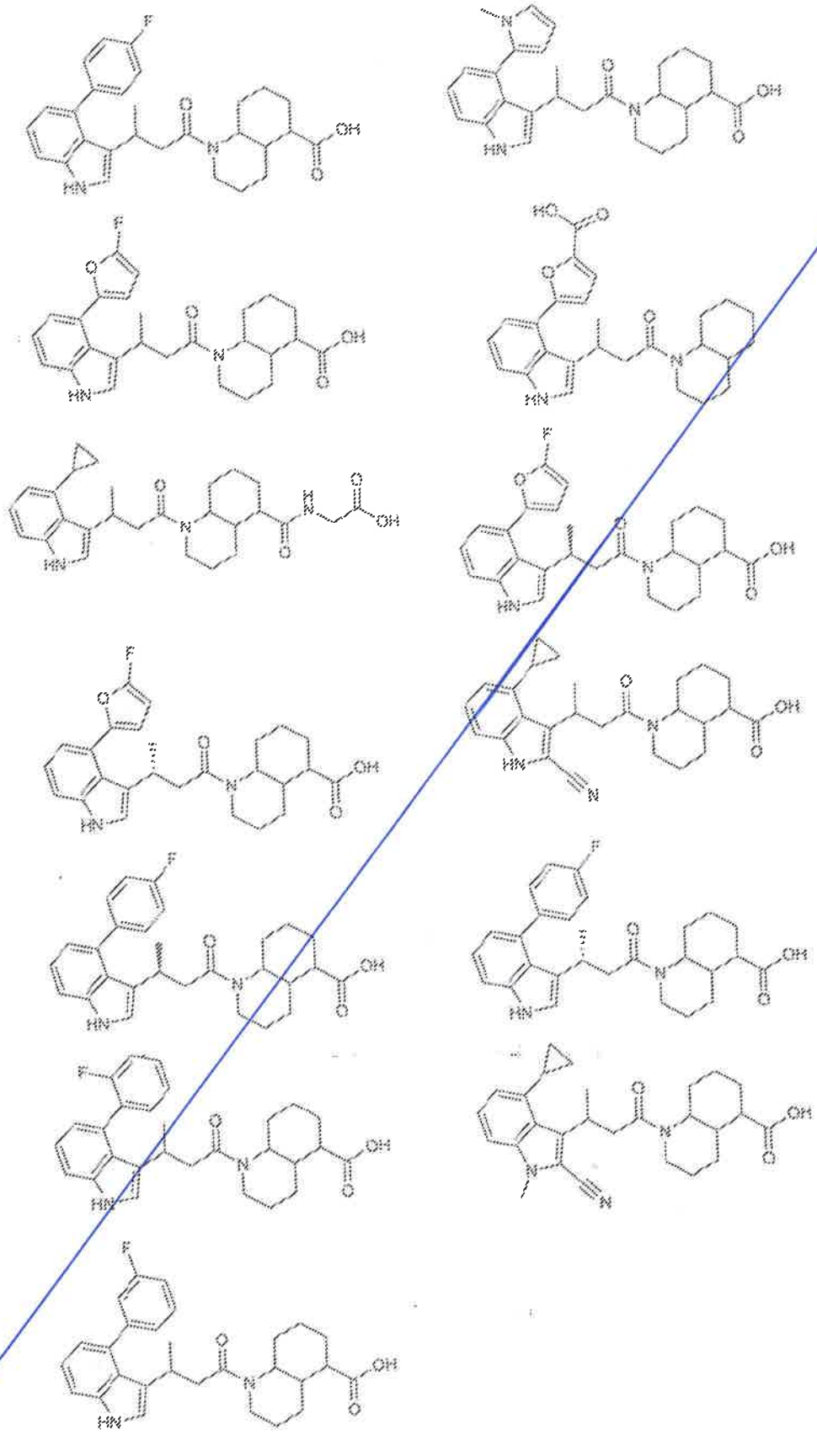















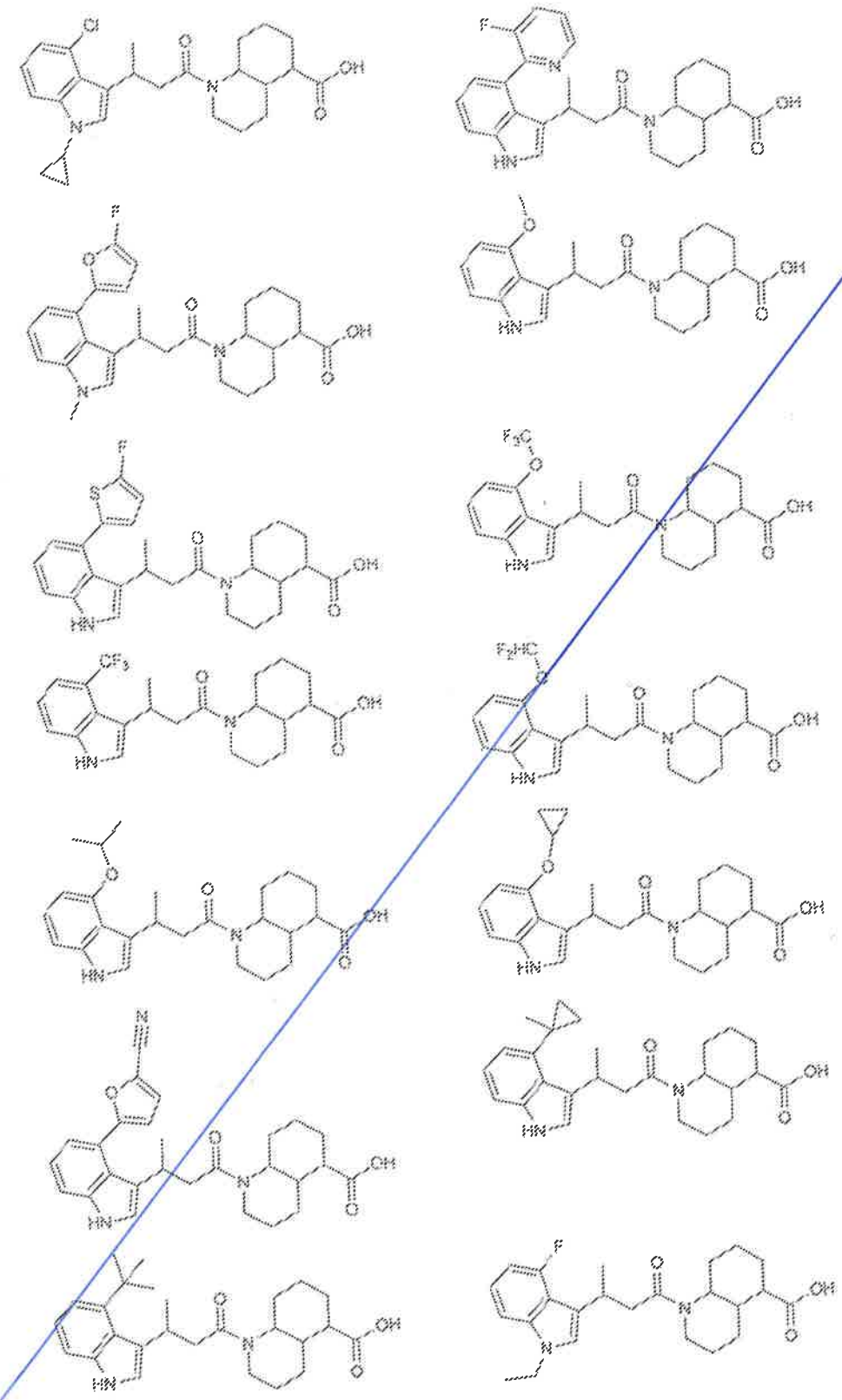


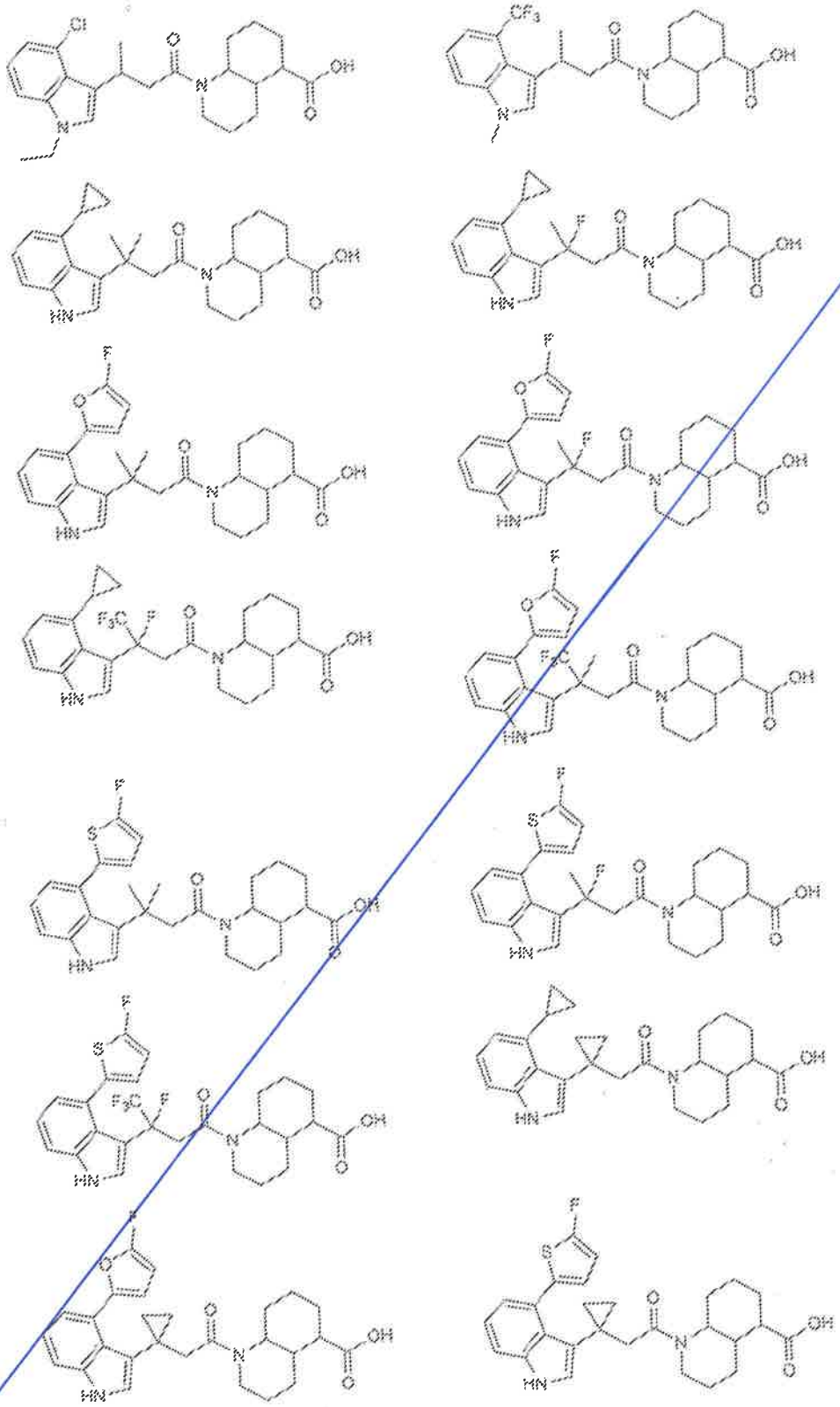


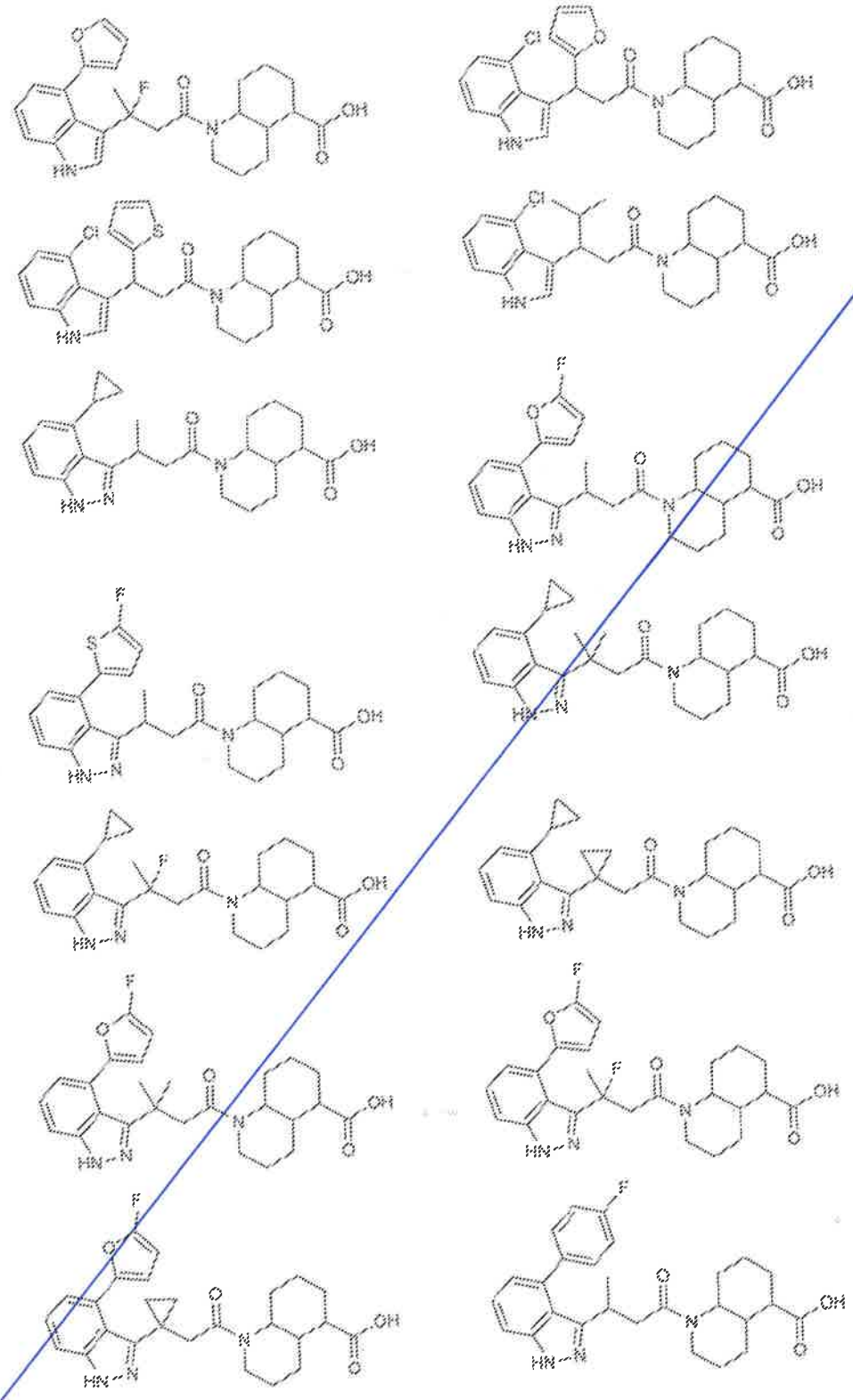















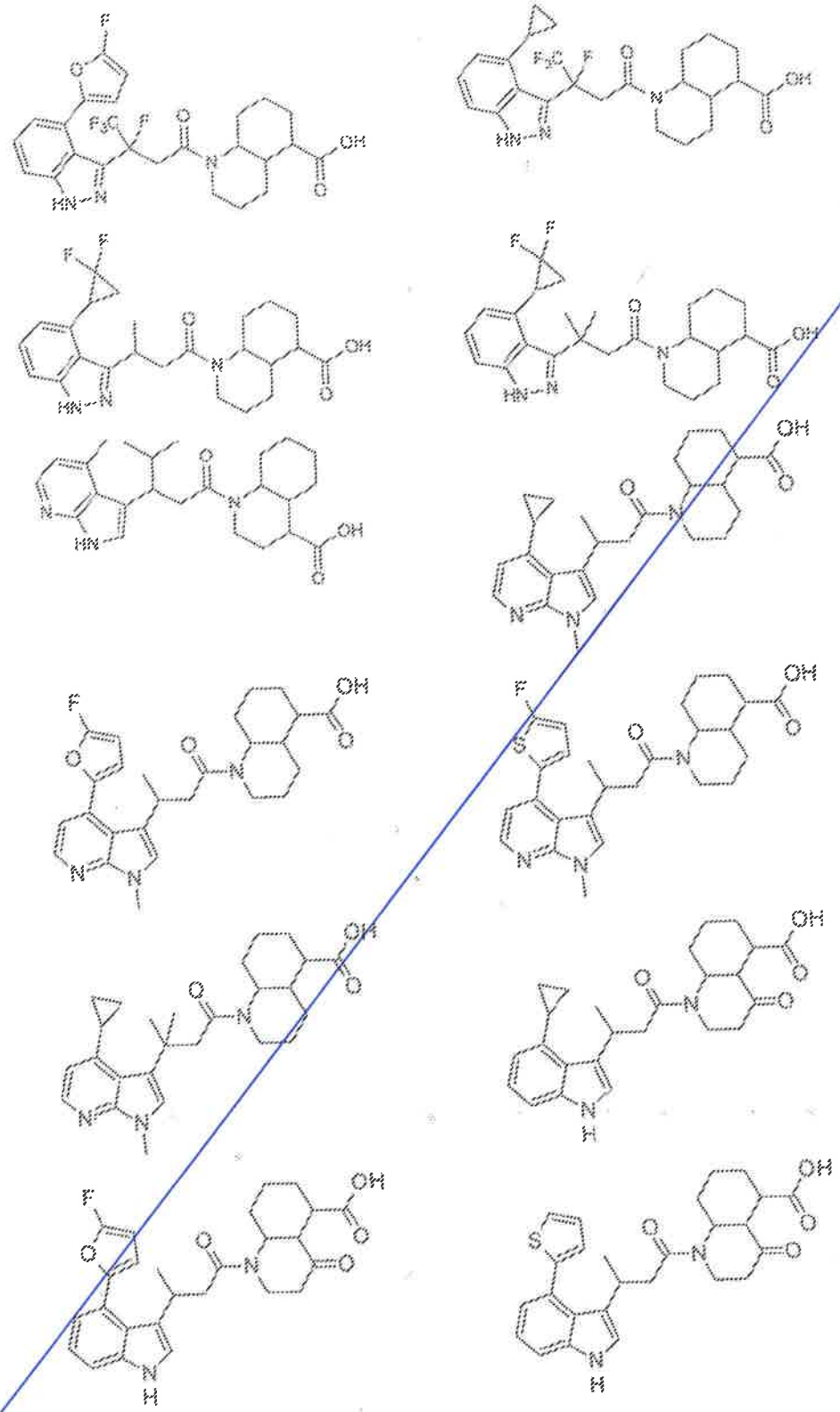


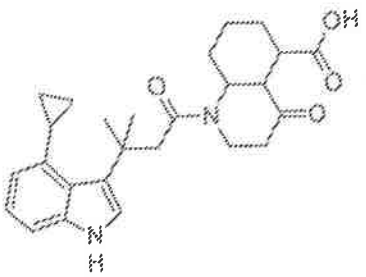
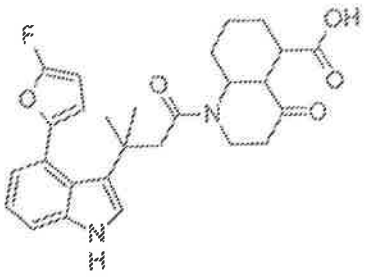
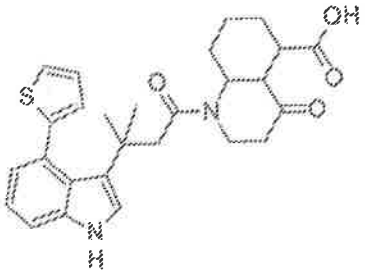
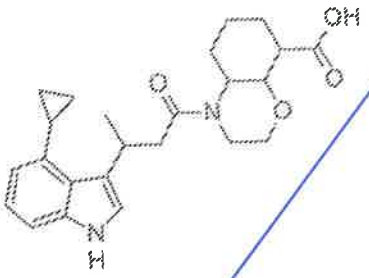
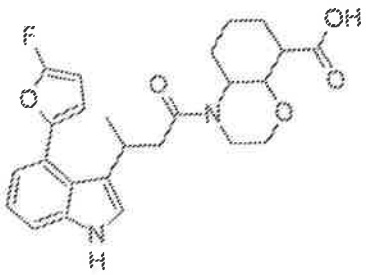
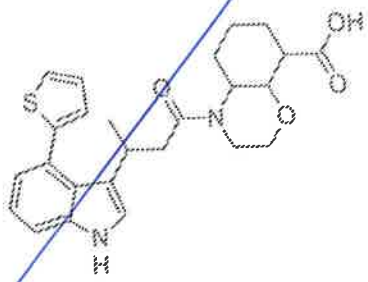
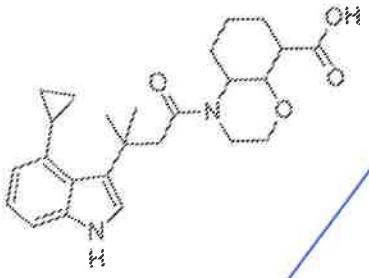
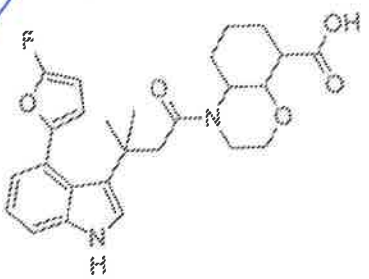
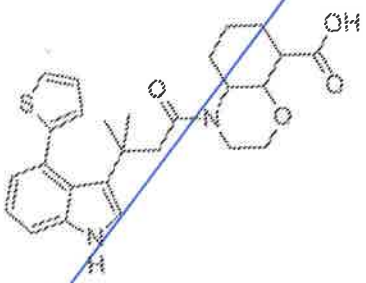
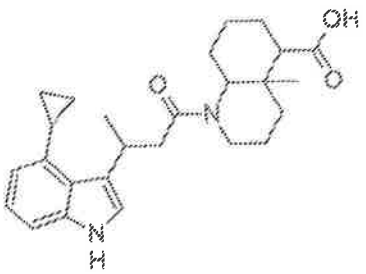
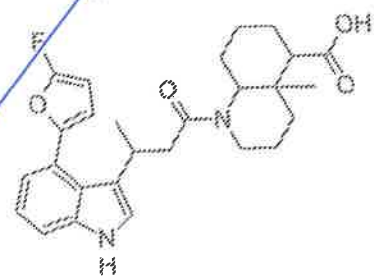
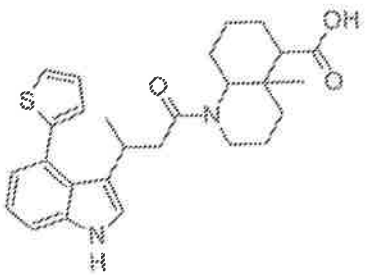


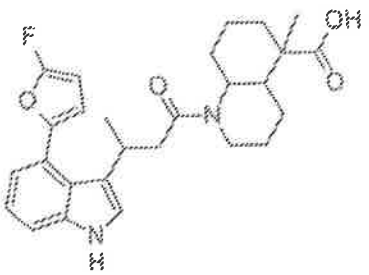
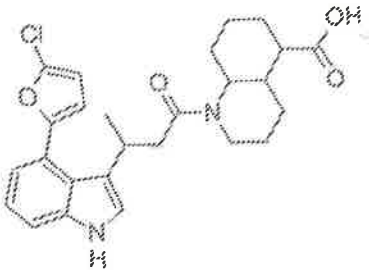
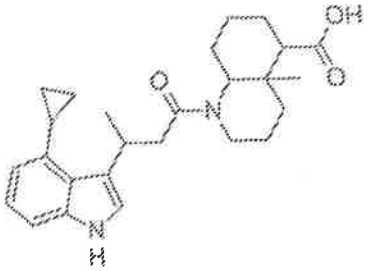
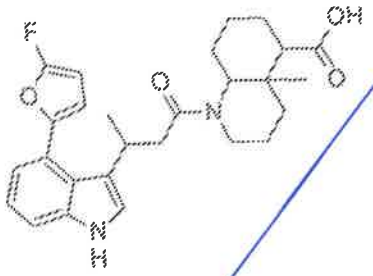
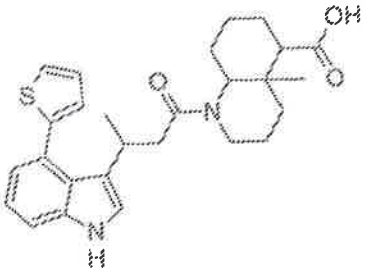
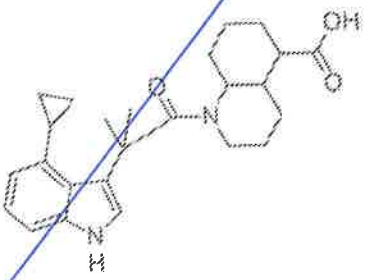
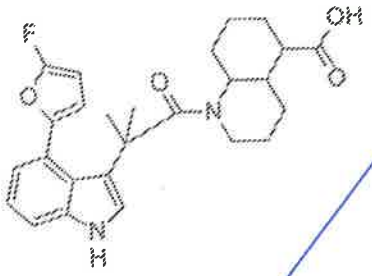
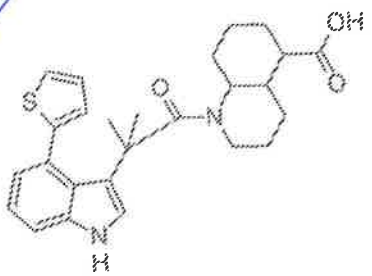
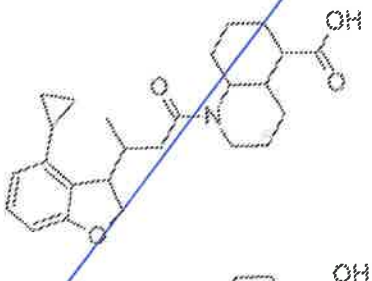
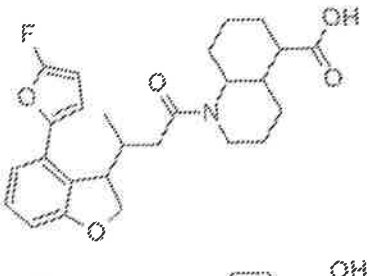
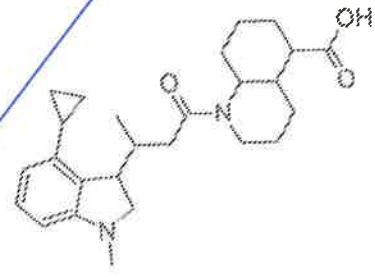
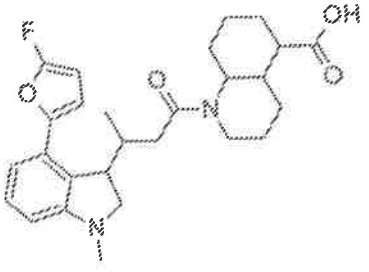


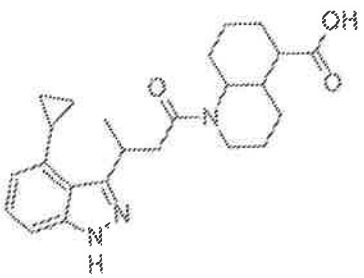
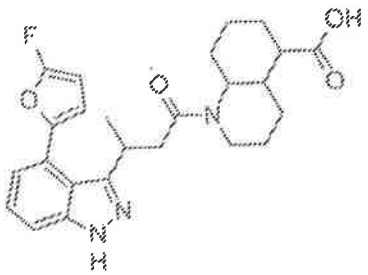
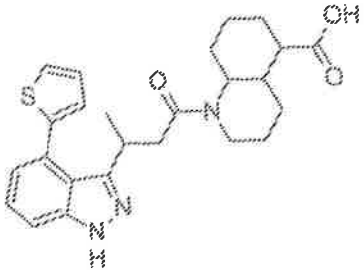
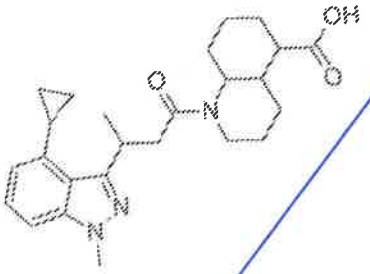
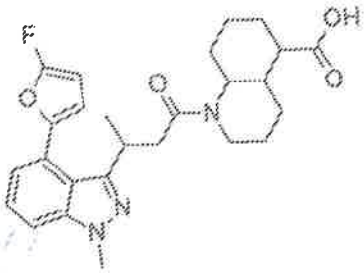
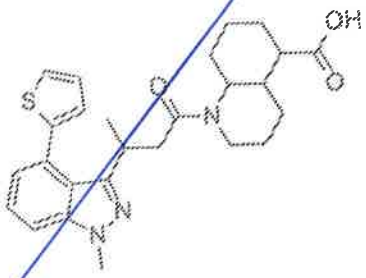
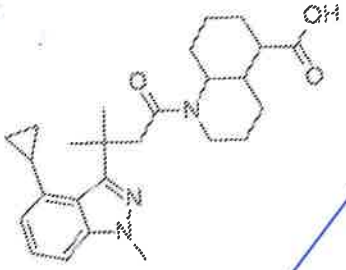
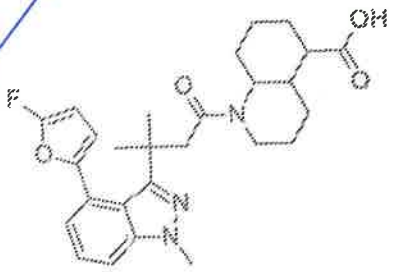
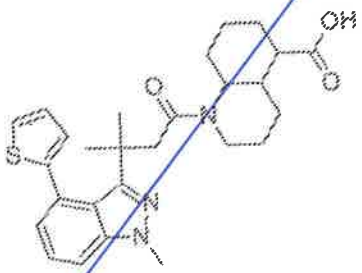
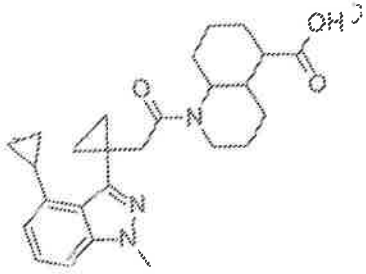
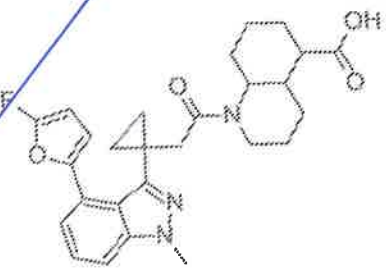
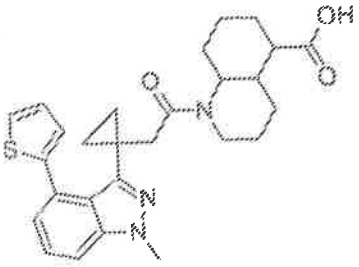


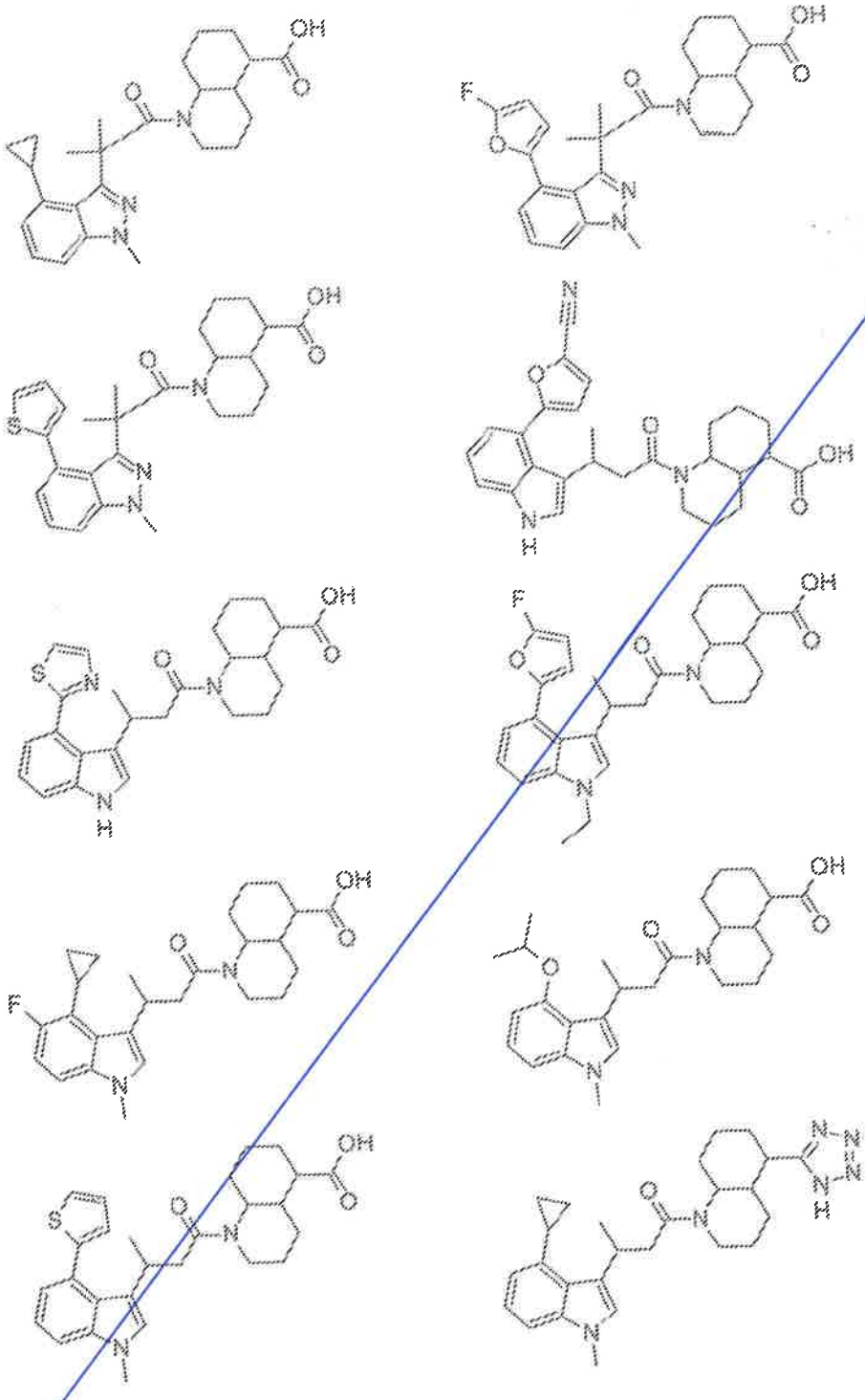


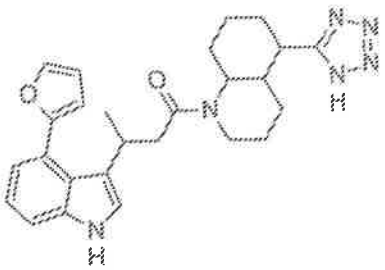


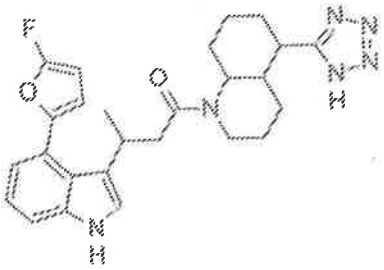













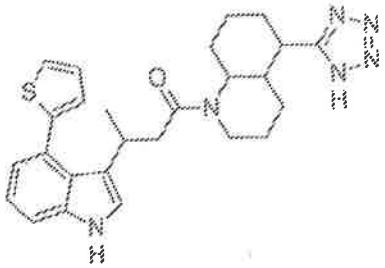













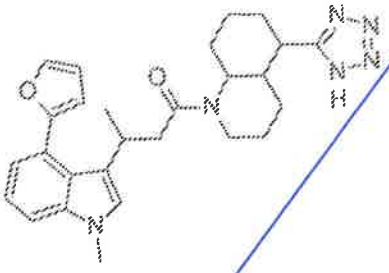













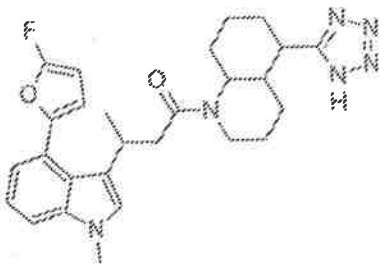


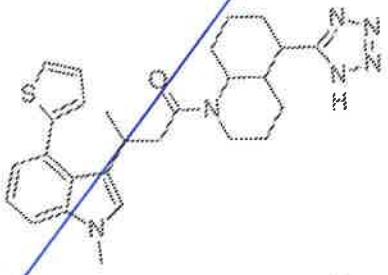


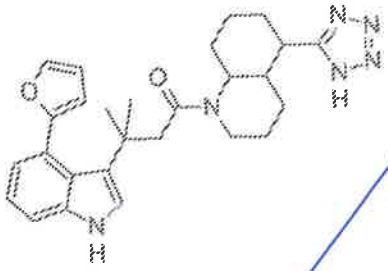


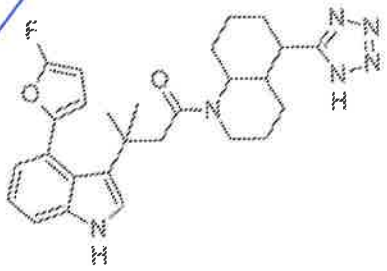


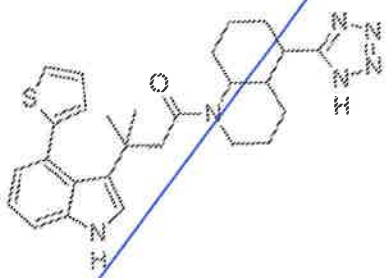


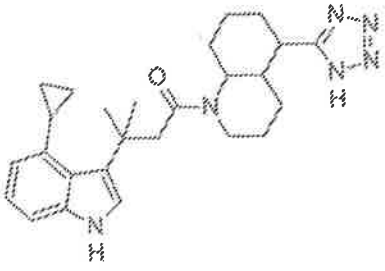


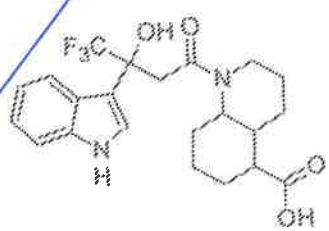


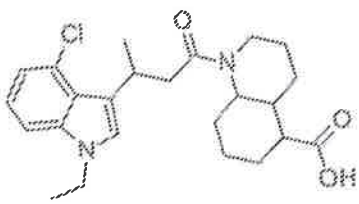


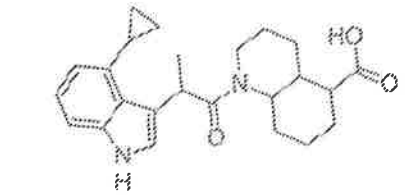
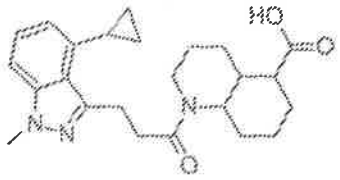
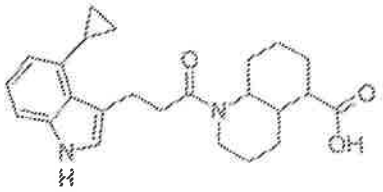
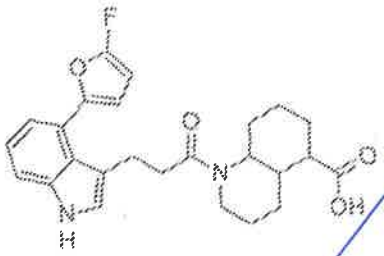
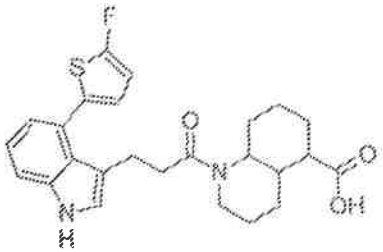
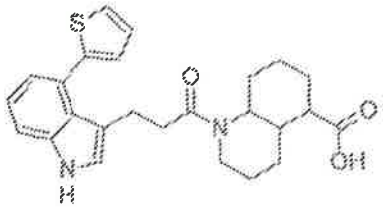










or pharmaceutically acceptable salt thereof.

10. A pharmaceutical composition including a compound according to any one of claims 1 to 9 and a pharmaceutically acceptable diluent, excipient or carrier.

11. A method of prevention or treatment of a condition in a mammal, the method comprising administering an effective amount of a compound according to any one of claims 1 to 9.

12. A method according to claim 11 wherein the condition can be prevented or treated by inhibition of 11β-HSD1.

13. A method according to claim 12 wherein the condition is selected from the group consisting of diabetes, hyperglycemia, low glucose tolerance, hyperinsulinemia, hyperlipidemia, hypertriglyceridemia, hypercholesterolemia, dyslipidemia, obesity, abdominal obesity, glaucoma, hypertension, atherosclerosis and its sequelae, retinopathy, nephropathy, neuropathy, osteoporosis, osteoarthritis, dementia, depression, neurodegenerative disease, psychiatric disorders, Cushing's Disease, Cushing's syndrome, viral diseases, and inflammatory diseases.

14. A method according to claim 13 wherein the condition is diabetes.

15. A method according to claim 14 wherein the condition is type II diabetes.

16. The method of claim 12, wherein the compound is administered in combination with an adjuvant.

17. The method of claim 16, wherein the adjuvant is selected from the group consisting of dipeptidyl peptidase-IV (DP-IV) inhibitors; (b) insulin sensitizing agents; (c) insulin and insulin mimetics; (d) sulfonylureas and other insulin secretagogues; (e) alpha-glucosidase inhibitors; (f) GLP-1, GLP-1 analogs, and GLP-1 receptor agonists; and combinations thereof.

18. The method of claim 17, wherein the insulin sensitizing agents are selected from the group consisting of (i) PPAR-gamma-agonists, (ii) PPAR-alpha-agonists, (iii) PPAR-alpha/gamma-dual agonists, (iv) biguanides, and combinations thereof.

19. Use of a compound according to claim 1 in the preparation of a medicament.

20. A use according to claim 19 wherein the medicament is for treatment of a condition that can be prevented or treated by inhibition of 11β-HSD1.

21. A use according to claim 20 wherein the condition is selected from the group consisting of diabetes, hyperglycemia, low glucose tolerance, hyperinsulinemia, hyperlipidemia, hypertriglyceridemia, hypercholesterolemia, dyslipidemia, obesity, abdominal obesity, glaucoma, hypertension, atherosclerosis and its sequelae, retinopathy, nephropathy, neuropathy, osteoporosis, osteoarthritis, dementia, depression, neurodegenerative disease, psychiatric disorders, Cushing's Disease, Cushing's syndrome, virus diseases, and inflammatory diseases.

22. A use according to claim 21 wherein the condition is diabetes.

23. A use according to claim 22 wherein the condition is type II diabetes.

24. A use according to claim 22 or 23, wherein the medicament contains an adjuvant.

25. A use according to claim 24, wherein the adjuvant is selected from the group consisting of dipeptidyl peptidase-IV (DP-IV) inhibitors; (b) insulin sensitizing agents; (c) insulin and insulin mimetics; (d) sulfonylureas and other insulin secretagogues; (e) alpha.-glucosidase inhibitors; (f) GLP-1, GLP-1 analogs, and GLP-1 receptor agonists; and combinations thereof.

26. A use according to claim 25 wherein the insulin sensitizing agents are selected from the group consisting of (i) PPAR-gamma-agonists, (ii) PPAR-alpha-agonists, (iii) PPAR-alpha/gamma-dual agonists, (iv) biguanides, and combinations thereof.