

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To: NICOLE M. BEELER
MERCK SHARP & DOHME CORP.
126 EAST LINCOLN AVENUE
RAHWAY, NJ 07065-0907

Date of mailing
(day/month/year)

17 DEC 2020

Applicant's or agent's file reference
24763

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/US 20/45693

International filing date (day/month/year)

11 August 2020 (11.08.2020)

Priority date (day/month/year)

13 August 2019 (13.08.2019)

International Patent Classification (IPC) or both national classification and IPC

IPC - A61K 31/436; A61K 31/4375; A61K 9/00 (2020.01)

CPC - A61K 31/436; A61K 31/4375; A61K 45/06

Applicant MERCK SHARP & DOHME CORP.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450
Facsimile No. 571-273-8300

Date of completion of this opinion

25 October 2020

Authorized officer

Lee Young

PCT Help Desk

Telephone No. 571-272-4300

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US 20/45693

Box No. 1 Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:

- ☒ the international application in the language in which it was filed.
- ☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(b)).

3. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:

a. ☐ forming part of the international application as filed:

☐ in the form of an Annex C/ST.25 text file.

☐ on paper or in the form of an image file.

b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

c. ☐ furnished subsequent to the international filing date for the purposes of international search only:

☐ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).

☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US 20/45693

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement

I. Statement

Novelty (N)	Claims	1-27	YES
	Claims	None	NO
Inventive step (IS)	Claims	10-14,19	YES
	Claims	1-9,15-18,20-27	NO
Industrial applicability (IA)	Claims	1-27	YES
	Claims	None	NO

2. Citations and explanations:

Claims 1-9, 15-18 and 20-27 lack an inventive step under PCT Article 33(3) as being obvious over WO 2017/196697 A1 to Merck Sharp and Dohme Corp. (hereinafter 'MERCK').

Regarding claim 1, Merck teaches an implant drug delivery system (pg 2, In 20-22, This invention relates to novel implant drug delivery systems for long-acting delivery of antiviral drugs. These compositions are useful for the treatment or prevention of human immunodeficiency virus (HIV) infection) comprising: (a) a core comprising a biocompatible nonerodible polymer and 4'-ethynyl-2-fluoro-2'-deoxyadenosine anhydrate (pg 3, In 10-16, Specifically, this invention relates to novel implant drug delivery systems comprising a biocompatible nonerodible polymer and 4'-ethynyl-2-fluoro-2'-deoxyadenosine), which is present in the core between 1% to 60% by weight (pg 8, In 3-32, In an embodiment of the implant drug delivery system described herein, the antiviral agent is present in the biocompatible nonerodible polymer at about 0.10%-80% by weight of drug loading) and (b) a biocompatible nonerodible diffusional barrier comprising a polymer (pg 4, In 18-23, As used herein, the term "diffusional barrier" refers to a coating that is permeable to the drug and is placed over at least a portion of the device to further regulate the rate of release. For example, a coating of biocompatible nonerodible polymeric material, e.g., EVA, or a coating of a biocompatible nonerodible polymeric material with a lower drug loading than the remainder of the implant delivery system, may be used) wherein said implant drug delivery system is implanted subdermally and 4'-ethynyl-2-fluoro-2'-deoxyadenosine anhydrate is continually released in vivo at a rate resulting in a plasma concentration of 4'-ethynyl-2-fluoro-2'-deoxyadenosine between 0.02 ng/mL and 300.0 ng/mL (pg 3, In 10-16, Specifically, this invention relates to novel implant drug delivery systems comprising a biocompatible nonerodible polymer and 4'-ethynyl-2-fluoro-2'-deoxyadenosine wherein said implant drug delivery system is implanted subdermally; see also pg 10, In 8-19, The implant drug delivery systems described herein are capable of releasing 4'-ethynyl-2-fluoro-2'-deoxyadenosine resulting in a plasma concentration of between 0.02-300 ng/mL per day) for a period of six months to thirty-six months (pg 9, In 24-33, The implant drug delivery systems described herein are capable of releasing 4'-ethynyl-2-fluoro-2'-deoxyadenosine over a period of 21 days, 28 days, 31 days, 4 weeks, 6 weeks, 8 weeks, 12 weeks, one month, two months, three months, four months, five months, six months, seven months, eight months, nine months, ten months, eleven months, twelve months, eighteen months, twenty-four months or thirty-six months), but Merck does not teach wherein said diffusional barrier has a thickness between 50 micrometer and 300 micrometer and Merck does not specifically teach 4'-ethynyl-2-fluoro-2'-deoxyadenosine anhydrate. However, it would have been obvious to a person having ordinary skill in the art to prepare the implant device wherein the diffusional barrier has a thickness of 50 micrometer by routine experimentation in order to optimize the delivery of the active agent. It would have been further obvious to select the anhydrate form of 4'-ethynyl-2-fluoro-2'-deoxyadenosine in order to select the form with the preferred pharmacokinetic profile to develop and commercialize the invention of Merck.

Regarding claim 2, Merck teaches the implant drug delivery system of Claim 1 (see above discussion). Merck further teaches wherein the 4'-ethynyl-2-fluoro-2'-deoxyadenosine plasma concentration is between 0.02 ng/mL and 30.0 ng/mL (pg 10, In 8-19, In an embodiment of the invention, the implant drug delivery systems described herein are capable of releasing 4'-ethynyl-2-fluoro-2'-deoxyadenosine resulting in a plasma concentration of between 0.02-30.0 ng/mL per day).

Regarding claim 3, Merck teaches the implant drug delivery system of Claim 2. Merck further teaches wherein the 4'-ethynyl-2-fluoro-2'-deoxyadenosine plasma concentration is between 0.02 ng/mL and 8.0 ng/mL (pg 10, In 8-19, In a further class of the embodiment, the implant drug delivery systems described herein are capable of releasing 4'-ethynyl-2-fluoro-2'-deoxyadenosine resulting in a plasma concentration of between 0.02-8.0 ng/mL per day).

Regarding claim 4, Merck teaches the implant drug delivery system of Claim 1 (see above discussion). Merck further teaches wherein the 4'-ethynyl-2-fluoro-2'-deoxyadenosine anhydrate is present in the core between 10% to 60% by weight (pg 8, In 3-32, In an embodiment of the implant drug delivery system described herein, the antiviral agent is present in the biocompatible nonerodible polymer at about 0.10%-80% by weight of drug loading).

Regarding claim 5, Merck teaches the implant drug delivery system of Claim 4. Merck further teaches wherein the 4'-ethynyl-2-fluoro-2'-deoxyadenosine anhydrate is present in the core at 15% to 40% by weight (pg 8, In 3-32, In an embodiment of the implant drug delivery system described herein, the antiviral agent is present in the biocompatible nonerodible polymer at about 0.10%-80% by weight of drug loading).

--continued in first supplemental box--

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US 20/45693

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

--BOX V.2 - CITATIONS AND EXPLANATIONS--

Regarding claim 6, Merck teaches the implant drug delivery system of Claim 4. Merck further teaches wherein the 4'-ethynyl-2-fluoro-2'-deoxyadenosine anhydrate is present in the core at about 40% by weight (pg 8, In 3-32, In other embodiments, the antiviral agent is present in the biocompatible nonerodible polymer at about... 40%-45% by weight of drug loading).

Regarding claim 7, Merck teaches the implant drug delivery system of Claim 4. Merck further teaches wherein the 4'-ethynyl-2-fluoro-2'-deoxyadenosine anhydrate is present in the core at about 60% by weight (pg 8, In 3-32, In other embodiments, the antiviral agent is present in the biocompatible nonerodible polymer at about... 40%-60% by weight of drug loading).

Regarding claim 8, Merck teaches the implant drug delivery system of Claim 1 (see above discussion). Merck further teaches wherein the biocompatible nonerodible polymer in the core is consisting of ethylene vinylacetate copolymer (EVA) (pg 3, In 30-33, Biocompatible nonerodible polymers of the instant invention include, but are not limited to, ethylene vinyl acetate copolymer (EVA)).

Regarding claim 9, Merck teaches the implant drug delivery system of Claim 8. Merck further teaches wherein the biocompatible nonerodible polymer in the core is consisting of poly(urethane) (pg 3, In 30-33, Biocompatible nonerodible polymers of the instant invention include, but are not limited to... poly(urethane)).

Regarding claim 15, Merck teaches the implant drug delivery system of Claim 1 (see above discussion). Merck further teaches a diffusional barrier (pg 4, In 18-23, As used herein, the term "diffusional barrier" refers to a coating that is permeable to the drug and is placed over at least a portion of the device to further regulate the rate of release. For example, a coating of biocompatible nonerodible polymeric material, e.g., EVA, or a coating of a biocompatible nonerodible polymeric material with a lower drug loading than the remainder of the implant delivery system, may be used), but Merck does not teach wherein said diffusional barrier has a thickness between 50 micrometer and 300 micrometer. However, it would have been obvious to a person having ordinary skill in the art to prepare the implant device wherein the diffusional barrier has a thickness of 50 micrometer by routine experimentation in order to develop and commercialize the invention of Merck.

Regarding claim 16, Merck teaches the implant drug delivery system of Claim 1 (see above discussion). Merck further teaches wherein the core and the biocompatible nonerodible diffusional barrier both comprise poly(urethane) (pg 4, In 10-17, In a class of the invention, the biocompatible nonerodible polymer is poly(urethane); see also pg 4, In 24-33, In a class of the invention, the diffusional barrier is poly(urethane)).

Regarding claim 17, Merck teaches the implant drug delivery system of Claim 1 (see above discussion). Merck further teaches wherein the core and the biocompatible nonerodible diffusional barrier are prepared by co-extrusion (pg 4, In 18-23, The diffusional barrier may be formed, for example, by coextrusion with the device), and Merck further teaches wherein extrusion is carried out at a temperature of 100-140 degrees C (pg 10, In 25-31, Implants were prepared using an extrusion process. The micronized polymer, and 4'-ethynyl-2-fluoro-2'-deoxyadenosine were blended at various ratios: 30, 35, 40, 45 and 50wt% drug in EVA. The preblend was melt extruded with a twin screw extruder at temperatures ranging from 100-140 degrees C, screw speed at 30 rpm, and then pelletized. The pellets were then 30 extruded with a single screw extruder with temperatures ranging from 110-140 degrees C), but Merck does not specifically teach the temperature of the co-extrusion, thus Merck does not teach wherein the co-extrusion is carried out at a temperature between 130 degrees C and 190 degrees C. However, it would have been obvious to a person having ordinary skill in the art to carry out the co-extrusion at 130 degrees C by routine experimentation in order to develop and commercialize the invention of Merck.

Regarding claim 18, Merck teaches the implant drug delivery system of Claim 1 (see above discussion). Merck further teaches wherein the core and the biocompatible nonerodible diffusional barrier are prepared by co-extrusion (pg 4, In 18-23, The diffusional barrier may be formed, for example, by coextrusion with the device), and Merck further teaches wherein extrusion is carried out at a temperature of 100-140 degrees C (pg 10, In 25-31, Implants were prepared using an extrusion process. The micronized polymer, and 4'-ethynyl-2-fluoro-2'-deoxyadenosine were blended at various ratios: 30, 35, 40, 45 and 50wt% drug in EVA. The preblend was melt extruded with a twin screw extruder at temperatures ranging from 100-140 degrees C, screw speed at 30 rpm, and then pelletized. The pellets were then 30 extruded with a single screw extruder with temperatures ranging from 110-140 degrees C), but Merck does not specifically teach the temperature of the co-extrusion, thus Merck does not teach wherein the co-extrusion is carried out at a temperature between 130 degrees C and 160 degrees C. However, it would have been obvious to a person having ordinary skill in the art to carry out the co-extrusion at 130 degrees C by routine experimentation in order to develop and commercialize the invention of Merck.

Regarding claim 20, Merck teaches the implant drug delivery system of Claim 1 (see above discussion). Merck further teaches the implant comprising between 1% and 20% by weight of a radiopaque material (pg 5, In 12-16, Optionally, the novel implant delivery systems of the instant invention can further comprise a radiopaque component. The radiopaque component will cause the implant to be Xray visible; see also pg 5, In 17-22, In another embodiment, the radiopaque material is about 1% to 20% by weight).

Regarding claim 21, Merck teaches the implant drug delivery system of Claim 20. Merck further teaches wherein the radiopaque material is barium sulfate (pg 5, In 12-16, Optionally, the novel implant delivery systems of the instant invention can further comprise a radiopaque component. The radiopaque component will cause the implant to be Xray visible. The radiopaque component can be any such element known in the art, such as barium sulphate).

Regarding claim 22, Merck teaches the implant drug delivery system of Claim 1 (see above discussion). Merck further teaches wherein the 4'-ethynyl-2-fluoro-2'-deoxyadenosine is released at therapeutic concentrations for a duration from between twenty-four months and thirty-six months (pg 9, In 24-33, The implant drug delivery systems described herein are capable of releasing 4'-ethynyl-2-fluoro-2'-deoxyadenosine over a period of... twenty-four months or thirty-six months... In an embodiment of the invention, the 4'-ethynyl-2-fluoro-2'-deoxyadenosine is released at therapeutic concentrations for a duration from between three months and thirty-six months).

--continued in next supplemental box--

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US 20/45693

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

--previous supplemental box--

Regarding claim 23, Merck teaches the implant drug delivery system of Claim 1 (see above discussion). Merck further teaches a method of treating or preventing HIV infection with an implant drug delivery system (pg 2, In 20-22. This invention relates to novel implant drug delivery systems for long-acting delivery of antiviral drugs. These compositions are useful for the treatment or prevention of human immunodeficiency virus (HIV) infection).

Regarding claim 24, Merck teaches an implant drug delivery system (pg 2, In 20-22. This invention relates to novel implant drug delivery systems for long-acting delivery of antiviral drugs. These compositions are useful for the treatment or prevention of human immunodeficiency virus (HIV) infection) comprising: (a) a core comprising a biocompatible nonerodible polymer and 4'-ethynyl-2-fluoro-2'-deoxyadenosine anhydride (pg 3, In 10-16. Specifically, this invention relates to novel implant drug delivery systems comprising a biocompatible nonerodible polymer and 4'-ethynyl-2-fluoro-2'-deoxyadenosine), which is present in the core between 1% to 60% by weight (pg 8, In 3-32. In an embodiment of the implant drug delivery system described herein, the antiviral agent is present in the biocompatible nonerodible polymer at about 0.10%-80% by weight of drug loading) and (b) a biocompatible nonerodible diffusional barrier comprising a polymer (pg 4, In 18-23. As used herein, the term "diffusional barrier" refers to a coating that is permeable to the drug and is placed over at least a portion of the device to further regulate the rate of release. For example, a coating of biocompatible nonerodible polymeric material, e.g., EVA, or a coating of a biocompatible nonerodible polymeric material with a lower drug loading than the remainder of the implant delivery system, may be used) wherein said 4'-ethynyl-2-fluoro-2'-deoxyadenosine anhydride has an in vitro release rate of 0.03 to 0.07 mg/day when measured between one and six months (pg 9, In 24-33. The implant drug delivery systems described herein are capable of releasing 4'-ethynyl-2-fluoro-2'-deoxyadenosine over a period of 21 days, 28 days, 31 days, 4 weeks, 6 weeks, 8 weeks, 12 weeks, one month, two months, three months, four months, five months, six months, seven months, eight months, nine months, ten months, eleven months, twelve months, eighteen months, twenty-four months or thirty-six months at an average rate of between 0.02-8.0 ng per day), but Merck does not teach wherein said diffusional barrier has a thickness between 50 micrometer and 300 micrometer and Merck does not specifically teach 4'-ethynyl-2-fluoro-2'-deoxyadenosine anhydride. However, it would have been obvious to a person having ordinary skill in the art to prepare the implant device wherein the diffusional barrier has a thickness of 50 micrometer by routine experimentation in order to optimize the delivery of the active agent. It would have been further obvious to select the anhydride form of 4'-ethynyl-2-fluoro-2'-deoxyadenosine in order to select the form with the preferred pharmacokinetic profile to develop and commercialize the invention of Merck.

Regarding claim 25, Merck teaches the implant drug delivery system of Claim 24. Merck further teaches wherein 4'-ethynyl-2-fluoro-2'-deoxyadenosine anhydride has an in vitro release rate of 0.08 mg/day when measured at day 30 (pg 12, Table 3, col 1, row 2, 35wt% EFdA + 65wt% EVA), but Merck does not specifically teach a release rate of 0.07 mg/day. However, it would have been obvious to a person having ordinary skill in the art to prepare the implant device which displays a release rate of 0.07 mg/day by routine experimentation in order to identify the implant device with the optimum pharmacokinetic profile for development and commercialization.

Regarding claim 26, Merck teaches the implant drug delivery system of Claim 24. Merck further teaches wherein 4'-ethynyl-2-fluoro-2'-deoxyadenosine anhydride has an in vitro release rate of 0.03 mg/day when measured at day 30 (pg 12, Table 3, col 1, row 1, 30wt% EFdA + 70wt% EVA), but Merck does not specifically teach a release rate of 0.04 mg/day. However, it would have been obvious to a person having ordinary skill in the art to prepare the implant device which displays a release rate of 0.04 mg/day by routine experimentation in order to identify the implant device with the optimum pharmacokinetic profile for development and commercialization.

Regarding claim 27, Merck teaches the implant drug delivery system of Claim 24. Merck further teaches wherein 4'-ethynyl-2-fluoro-2'-deoxyadenosine anhydride has an in vitro release rate of 0.03 mg/day when measured at day 30 (pg 12, Table 3, col 1, row 1, 30wt% EFdA + 70wt% EVA).

Claims 10-14 and 19 meet the criteria set out under PCT Article 33(2)-(3) because the prior art does not teach or fairly suggest the claimed invention.

Regarding claim 10, Merck teaches the implant drug delivery system of Claim 1 (see above discussion). Merck further teaches a diffusional barrier comprising a polymer (pg 4, In 18-23. As used herein, the term "diffusional barrier" refers to a coating that is permeable to the drug and is placed over at least a portion of the device to further regulate the rate of release. For example, a coating of biocompatible nonerodible polymeric material, e.g., EVA, or a coating of a biocompatible nonerodible polymeric material with a lower drug loading than the remainder of the implant delivery system, may be used) and Merck also teaches wherein the polymer is hydrophobic (pg 3, In 17-29. The polymer is generally hydrophobic so that it retains its integrity for a suitable period of time when placed in an aqueous environment, such as the body of a mammal, and stable enough to be stored for an extended period before use), but Merck does not teach wherein the diffusional barrier comprises a hydrophobic polymer with a soluble filler.

US 2005/0031668 A1 to Patel et al. (hereinafter 'PATEL') teaches an implant drug delivery system (para [0013] In one aspect, the invention provides an implantable device for administration of nalmefene to a mammal in need thereof, which includes nalmefene encapsulated in a biocompatible, nonerodible polymeric matrix) and Patel further teaches wherein the diffusional barrier comprises a hydrophobic polymer (para [0030] The release rate may also be modified by coating the exterior surface of the implant with a diffusional barrier, such as an erodible or non-erodible polymer, for example EVA; see also para [0025] As used herein, "nonerodible matrix" refers to a polymeric carrier that is sufficiently resistant to chemical and/or physical destruction by the environment of use such that the matrix remains essentially intact throughout the release period. The polymer is generally hydrophobic so that it retains its integrity for a suitable period of time when placed in an aqueous environment, such as the body of a mammal, and stable enough to be stored for an extended period before use), but Patel does not teach wherein the diffusional barrier comprises a hydrophobic polymer with a soluble filler. Therefore the prior art does not teach or fairly suggest the claimed invention.

--continued in next supplemental box--

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US 20/45693

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

--previous supplemental box--

Regarding claims 11-14, these claims depend on claim 10, thus these claims also meet the criteria set out under PCT Article 33(2)-(3).

Regarding claim 19, Merck teaches the implant drug delivery system of Claim 1 (see above discussion). Merck further teaches an implant device comprising 4'-ethynyl-2-fluoro-2'-deoxyadenosine (pg 3, In 10-16. Specifically, this invention relates to novel implant drug delivery systems comprising a biocompatible nonerodible polymer and 4'-ethynyl-2-fluoro-2'-deoxyadenosine) and Merck further teaches X-ray opacity (pg 5, In 12-16. Optionally, the novel implant delivery systems of the instant invention can further comprise a radiopaque component. The radiopaque component will cause the implant to be Xray visible) but Merck does not specifically teach 4'-ethynyl-2-fluoro-2'-deoxyadenosine anhydrate. It would have been obvious to a person having ordinary skill in the art to select the anhydrate form of 4'-ethynyl-2-fluoro-2'-deoxyadenosine by routine experimentation in order to select the form with the preferred pharmacokinetic profile to develop and commercialize the invention of Merck. However, it would not have been obvious to select the form that is characterized by a powder x-ray diffraction pattern with at least peaks at diffraction angles degrees 2 theta (+/- 0.2 degrees) 11.79, 12.39, 14.70 and 15.51 in a powder x-ray diffraction obtained using Cu K alpha radiation, because there is no obvious motivation for selecting this solid form.

Patel teaches wherein the implant is characterized for drug load and rate of release (para [0053] Extruded rods prepared as described above were characterized for total drug load and for rate of drug release), but Patel does not teach powder x-ray diffraction, thus Patel does not teach wherein 4'-ethynyl-2-fluoro-2'-deoxyadenosine anhydrate is characterized by a powder x-ray diffraction pattern with at least peaks at diffraction angles degrees 2 theta (+/- 0.2 degrees) 11.79, 12.39, 14.70 and 15.51 in a powder x-ray diffraction obtained using Cu K alpha radiation. Therefore the prior art does not teach or fairly suggest the claimed invention.

Claims 1-27 have industrial applicability as defined by PCT Article 33(4) because the subject matter can be made or used by industry.