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Expert Opinion
upon the results of
intellectual property expert research

19.01.2017 **No. 01-01/17**

On 23.12.2016 the letter of the attorney O.S. Mamunya on conducting the intellectual property expert research was received.

The following appendices were attached to the letter:

1. A copy of the description of the patent of Ukraine No. UA89220 for the invention “Method For Treatment Of HIV/AIDS By Administration Of Solid Pharmaceutical Dosage Formulation Comprising A HIV Protease Inhibitor In Fasted State” dated 11.01.2010, on 20 sheets. (Appendix 1).
2. Source 1 (D1) The International application WO 01/34119 published in accordance with the Patent Cooperation Treaty and translation of the Source 1 on 74 sheets.
3. Source 2 (D2) The International application WO 2005/039551 published in accordance with the Patent Cooperation Treaty (analogue UA85564) and translation of the Source 2 (in the edition of its analogue UA85564) on 75 sheets.
4. Source 3 (D3) Approved information on medicinal product "KALETRA" and translation of the Source 3 on 73 sheets.
5. Source 4 (S 4) Instruction for medical use of medicinal product “KALETRA” in tablets and translation of the Source 4 on 70 sheets.

The objects of the research:

- the invention “Method For Treatment Of HIV/AIDS By Administration Of Solid Pharmaceutical Dosage Formulation Comprising A HIV Protease Inhibitor In Fasted State” under the patent of Ukraine No. UA89220 dated 11.01.2010, details of which are contained in patent description - Appendix 1.
- provided for research materials on prior art of the invention, listed in the introduction and in the investigational part of the conclusion, D1-4.

The above documents were delivered by a courier.

The following question was introduced for the decision of the expert research.

"Does the invention under the patent of Ukraine No. 89220 comply with patentability requirements such as novelty, inventive level based on the prior art of the invention and documents published before the priority date?”

The research is conducted by an intellectual property representative, patent attorney of Ukraine, reg. No. 348, Andrieieva Aliona Victorivna who has a degree in economics and law, and has a special education in the field of intellectual property; educational qualifying level “specialist”, experience in conducting researches of the intellectual property items – 12 years (since 2005).

In the process of research the following regulatory acts, professional and reference materials were used:

1. *the Law of Ukraine No. 3687-XII dated December 15, 1993 " On Protection of Rights for Inventions and Utility Models » [E-resource] // Holos Ukrainy – 03.02.1994. [E-resource] // access mode to the law: http://zakon1.rada.gov.ua/laws/show/3687-12*

2. *Rules of consideration of the application for invention (utility model) No. 197 approved by the Ministry of education and science of Ukraine on 15.03.2002, registered in the Ministry of justice of Ukraine under No. 364/6652 on 15.04.2002 [E-resource] // access mode to the rule: http://zakon1.rada.gov.ua/laws/show/z0364-02*

3. *Rules for drafting and filing an application for invention and utility model No. 22. approved by the Ministry of education and science of Ukraine on 22.01.2001, registered in the Ministry of justice of Ukraine under No. 173/5364 on 27.02.2001 [E-resource] // access mode to the rule: http://zakon5.rada.gov.ua/laws/show/z0173-01/print*

4. *Krainiev P.P., Rabotiahova L.I., Diatlyk I.I. Patenting of inventions in Ukraine – K.: Publishing house «In-Yure», 2000. – 340 pages.*

5. *Krainiev P.P., Kovaliova N.M., Melnykov M.V. Court examinations in the field of intellectual property / Under editorship of Krainiev P.P.,. – Vinnitsa: PP «Printing center «Phoenix», DIVP OJSC «Infrakon» - «Infrakon-I», 2008. – 376 pages.*

6. *Methodological recommendations on certain issues of conducting examination of an application for invention (utility model) / SE «Ukrainian institute of industrial property». – Kyiv, 2014. – 141 pages.*

7. *Guidelines for conducting substantial examination. Part C [E-resource] // Guidelines on examination in European patent office. – April 2010. – 178 pages. - access mode: http://www.rupto.ru/rupto/nfile/a1228d52-4021-11e1-658a-9c8e9921fb2c/EPOExaminationGuidlinesPartC.pdf*

I. *RESEARCH*

The evidence belonging to the properties of the material and immaterial (information) objects were studied in the process of conducting the research on compliance with the requirements of the patentability.

The following was used to solve the set tasks:

a. *methods of contrast and comparison, synthesis and analysis*

b. *provisions of legal acts and literature listed in the previous section*

The specialist considers it appropriate to provide definitions of terms that are used during the research.

Invention (utility model) is the result of intellectual activity of a person in any field of technology [1].

According to Article 6 of the Law [1]: «2. This Law provides legal protection for the following objects of the invention: the product (device, substance, microorganism strain, culture of plant cells or animal cells, etc.; process (method), as well as new way of use of well-known product or process».

The extent of legal protection is defined by the formula of the invention, containing all its essential features. In other words, the formula of invention is a brief verbal description of the invention that contains the set of its essential characteristics [3, clause 7.1].

According to the clause 6.6.1. of the Rules [3]: "the essence of the invention is a combination of fundamental features sufficient to achieve a technical result which provides the invention (utility model)".

Formula of invention is a brief verbal description of the technical essence of invention that contains the set of its essential characteristics, sufficient for technical results that were specified by the applicant. Formula of the invention (utility model) should be based on the description, i.e. it should characterize the invention with the same concepts that were used as a description of the invention (utility model). [3, clause 6.3.].

According to the Rules [3]: «6.3.2.4. *Independent claim. Independent claim of the invention formula (utility model) must relate to only one invention (one utility model).*

General substantial characteristics of the invention, each of which is required in all cases, whether it is the implementation or use of the invention, and all together are sufficient to obtain technical result that is achieved in all cases, covered by the scope of legal protection that is requested, are included to the independent claim of the invention (or to each independent claim of the formula that characterizes a group of inventions).

While developing the independent claim of the formula it is necessary to take into account that the total of essential characteristics that are necessary and sufficient for achievement of the technical result must be described by a specific set of features inherent for this object.

The value of this formula of the invention consists in the fact that it is the sole criterion for determining the scope of the invention, namely the totality of objects that are subject to the rights of the patentee.

As to its structure the formula of the invention can be single-claim or multiclaim, and it may include one or several claims respectively. Single-claim formula of the invention is used for characterization of one invention by a number of essential characteristics that don't have development or clarification on individual cases of its implementation or use. Multiclaim formula of the invention (utility model) is used to characterize a single invention (utility model) with the development and (or) specification of the totality of its characteristics concerning some of cases of implementation and use of the invention or for characterization of a group of inventions. Multiclaim formula that characterizes one invention has one independent claim which is followed by depending claim(s). Multiclaim formula that characterizes a group of inventions, has several independent claims. Each of them characterizes one of the inventions of the group. While each of the inventions of the group can be characterized using the dependent claims, subordinated to the appropriate independent claim [3, claim 7.2]. So, the independent claim of the invention formula must relate to only one invention [3, claim 7.3.2].

Claims are divided into restrictive and distinctive parts. Notable features inherent for the prototype of the invention are placed in the first part (restrictive) of the formula, and the new ones, created by the inventor, are placed in the next part, the distinctive one. I.e., the restrictive part of the invention formula claim includes the substantial characteristics of the invention, which coincide with characteristics of the nearest analog (prototype), while distinctive part includes substantial characteristics that distinguish the invention from the prototype.

The characteristics are called substantial, when each of them are necessary, and all together they are sufficient to achieve technical result. In other words, the characteristics are substantial if they affect the technical result, i.e. are in cause-and-effect relationship with it [4, p. 121; 5, p. 125].

I. Description of the object of the research

A group of inventions under the patent of Ukraine No. UA89220 "Method For Treatment Of HIV/AIDS By Administration Of Solid Pharmaceutical Dosage Formulation Comprising A HIV Protease Inhibitor In Fasted State" is the object of the research.

Bibliographical data of a patent of Ukraine No. UA89220 for invention dated 10.02.2009

(11) Number of the patent	**UA89220**
(24) Date of registration	11.01.2010
(21) Application number	a200710440
(22) Filing date	21.02.2006
(24) Effective date	11.01.2010
(31) Number of the previous application filed in accordance with the Paris Convention	11/064,467
(32) Date of previous application filed in accordance with the Paris Convention	23.02.2005
(33) two-letter code of the country where the previous application was filed	US
(54) Name of	Method For Treatment Of HIV/AIDS By Administration Of Solid Pharmaceutical Dosage Formulation Comprising A HIV Protease Inhibitor In Fasted State
(73) Owner	ABBVIE INC. (US)

According to the patent of Ukraine No. UA89220 the claims have the following version:

«1. HIV/AIDS treatment, which includes the introduction of solid dosage form to patients who need treatment, provided that the specified dosed form is taken by the patient with no food or under conditions of fasting, and the specified dosage form contains lopinavir and ritonavir as a solid solution or solid dispersion;

pharmaceutically acceptable water-soluble polymer with glass transition temperature Tg = at least 50 °C and pharmaceutically acceptable surface-active agent with the value of hydrophilic-lipophilic balance (GLB) from 4 to 10.

2. Method according to claim 1, in which specified pharmaceutically acceptable surface active substance is selected from a simple polyoxyethylene alkyl ether, simple polyoxyethylene alkyl aryl ether, compound burkester, alkylene glycollic monocompound cetylated fatty acid ether, compound ether sucrosse fatty acid or monocompound ether of sorbitan fatty acid.

3. Method according to claim 1, in which the specified surface active substance is selected from polyoxyethylene (3) lauryl ether, polyoxyethylene (5) cetyl ether, polyoxyethylene (2) stearyl ether, polyoxyethylene (5) stearyl ether, polyoxyethylene (2) nonylphenyl ether, polyoxyethylene (3) nonylphenyl ether, polyoxyethylene (4) nonylphenyl ether, polyoxyethylene (3) octylphenyl ether, PEG-200 monolaurate, PEG-200 dilaurate, PEG-300 dilaurate, PEG-400 dilaurate, PEG-300 distearate, PEG-300 dioleate, propylene glycol monolaurate, sucrose monostearate, sucrose dystearate, sucrose monolaurate, sucrose dilaurate, sorbitan monolaurate, sorbitan monooleate, sorbitan monopalmitate or sorbitan stearate.

4. Method according to claim 1, where the specified surface-active material is a complex ether of sorbitan fatty acid.

5. Method according to claim 1, where the specified surface-active material is a sorbitan monolaurate.

6. Method according to claim 1, in which the specified water soluble polymer is extracted from N-vinyl lactam homopolymer, N-vinyl lactam copolymer, compound cellulose ester, simple cellulose ether, polyalkylene oxide, polyacrylate, polymethacrylate, polyacrylamide, polyvinyl alcohol, vinyl acetate polymer, oligosaccharide and polysaccharide.

7. Method according to claim 1, in which the specified water soluble polymer is extracted from N-vinylpyrrolidone homopolymer, copolymer of N-vinylpyrrolidone, copolymer of N-vinylpyrrolidone and vinyl acetate, copolymer of N-vinylpyrrolidone vinylor vinylpropionat, polyvinylpyrrolidone, methyl cellulose, ethyl cellulose ,hydroxyalkyl cellulose, hydroxypropyl cellulose, hydroxyalkyl cellulose, hydroxypropyl methylcellulose, cellulose phthalate, cellulose succinate, cellulose acetyl phthalate, hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose succinate, hydroxypropyl methylcellulose acetate succinate, polyethylene oxide, polypropylene oxide, ethylene oxide copolymer and propylene oxide, methacrylic acid / ethyl acrylate copolymer, methacrylic acid / methyl methacrylate copolymer, butyl methacrylate / copolymer of 2-dimethylaminoethyl methacrylate, poly (hydroxy alkyl acrylate), poly (hydroxy alkyl methyl acrylate), copolymer of vinyl acetate and crotonic acid, partially hydrolyzed polyvinyl acetate, carrageenan, galactomannan or xanthane gum.

8. Method according to claim 1, in which the specified pharmaceutically acceptable water-soluble polymer constitutes a mixed polymer of N-vinylpyrrolidone and vinyl acetate.

9. Method according to claim 1, in which the specified pharmaceutically acceptable water-soluble polymer constitutes a copovidone.

10. Method according to claim 1, in which the specified water soluble polymer is extracted from the group that consists of N-vinyl lactam homopolymer, N-vinyl lactam copolymer, compound cellulose ester, simple cellulose ether, polyalkylene oxide, polyacrylate, polymethacrylate, polyacrylamide, polyvinyl alcohol, vinyl acetate polymer, oligosaccharide and polysaccharide.

and in which specified pharmaceutically acceptable surface active substance is selected from a group that consists of simple polyoxyethylene alkyl ether, simple polyoxyethylene alkyl aryl ether, compound burkester, alkylene glycollic monocompound cetylated fatty acid ether, compound ether sucrosse fatty acid and monocompound ether of sorbitan fatty acid.

11. Method according to claim 1, in which the specified water soluble polymer is extracted from the group that consists of N-vinylpyrrolidone homopolymer, copolymer of N-vinylpyrrolidone, copolymer of N-vinylpyrrolidone and vinyl acetate, copolymer of N-vinylpyrrolidone or vinyl propionate, polyvinylpyrrolidone, methyl cellulose, ethyl cellulose, hydroxyalkyl cellulose, hydroxypropyl cellulose, hydroxyalkyl cellulose, hydroxypropyl methylcellulose, cellulose phthalate, cellulose succinate, cellulose acetyl phthalate, hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose succinate, hydroxypropyl methylcellulose succinate acetate, polyethylene oxide, polypropylene oxide, copolymer of ethylene oxide and propylene oxide, methacrylic acid / ethyl acrylate copolymer, methacrylic acid / methyl methacrylate copolymer, butyl methacrylate / copolymer of 2-dimethylaminoethyl methacrylate, poly (hydroxy alkyl acrylate), poly (hydroxy alkyl methyl acrylate), vinyl acetate and crotonic acid copolymer, partially hydrolyzed polyvinyl acetate, carrageenan, galactomannan and xanthane gum,

and where the specified surface active agent is choosen from the group which consists of polyoxyethylene (3) lauryl ether, polyoxyethylene (5) cetyl ether, polyoxyethylene (2) stearyl ether, polyoxyethylene (5) stearyl ether, polyoxyethylene (2) nonylphenyl ether, polyoxyethylene (3) nonylphenyl ether, polyoxyethylene (4) nonylphenyl ether, polyoxyethylene (3) octylphenyl ether, PEG-200 monolaurate, PEG-200 dilaurate, PEG-300 dilaurate, PEG-400 dilaurate, PEG-300 distearate, PEG-300 dioleate, propylene glycol monolaurate, sucrose monostearate, sucrose dystearate, sucrose monolaurate, sucrose dilaurate, sorbitan monolaurate, sorbitan monooleate, sorbitan mono palmitate, sorbitan stearate.

12. Method according to claim 1, in which specified dosed form contains 50-85 mass. % of the dosed form of specified water soluble polymer and 2-20 mass. % of dosed form of specified surface active substances.

13. Method according to claim 1, where the specified water soluble polymer is a copolymer of N-vinylpyrrolidone and vinyl acetate and the specified surface active substance is a complex ether of sorbitan fatty acid.

14. Method according to claim 1, where the specified water soluble polymer is a copovidone and the specified surface active substance is a sorbìtan monolaurate.

15. Method according to claim 14, in which the specified dosed form contains 50-85 mass. % of dosed form of specified water soluble polymer and 2-20 mass. % of dosed form of specified surface active substance.

16. Method according to claim 1, where the specified ritonavir and lopinavir are represented as solid dispersion.

17. Method according to claim 1, where the specified ritonavir and lopinavir are represented as solid solution.

18. Method according to claim 13, where the specified ritonavir and lopinavir are represented as solid dispersion.

19. Method according to claim 13, where the specified ritonavir and lopinavir are represented as solid solution.

20. Method according to claim 14, where the specified ritonavir and lopinavir are represented as solid dispersion.

21. Method according to claim 14 where the specified ritonavir and lopinavir are represented as solid solution.

22. Method according to claim 11, where the specified ritonavir and lopinavir are represented as solid dispersion.

23. Method according to claim 11, where the specified ritonavir and lopinavir are represented as solid solution.

24. Method according to claim 15, where the specified ritonavir and lopinavir are represented as solid solution.

25. HIV/AIDS treatment, which includes the introduction of solid dosage form to patients who need treatment, provided that the specified dosed form is taken by the patient with no food or under conditions of fasting, and the specified dosage form contains lopinavir and ritonavir as a solid solution or solid dispersion; pharmaceutically acceptable water-soluble polymer with glass transition temperature Tg = at least 50 °C and combinations of surface-active agents with the value of hydrophilic-lipophilic balance (GLB) from 4 to 10.

26. Method according to claim 25, where the specified ritonavir and lopinavir are represented as solid solution.

27. HIV/AIDS treatment, which includes the introduction of solid dosage form to patients who need treatment, provided that the specified dosed form is taken by the patient with no food or under conditions of fasting, and the specified dosage form contains non soluble form of lopinavir.

28. Method according to claim 27, in which the specified non-soluble form of lopinavir is presented in the form of lopinavir solid dispersion in the matrix, where the indicated matrix has at least one pharmaceutically acceptable water-soluble polymer and at least one pharmaceutically acceptable surface active substance and provided that the indicated pharmaceutically acceptable surface active substance contains surface active substance with the value of hydrophilic-lipophilic balance (GLB) from 4 to 10.

29. Method according to claim 28, in which at least one indicated pharmaceutically acceptable water-soluble polymer has glass transition temperature Tg of at least 50 °C.

30. Method according to claim 27, in which the specified non-soluble form of lopinavir is presented in the form of lopinavir solid solution in the matrix, where the indicated matrix has at least one pharmaceutically acceptable water-soluble polymer and at least one pharmaceutically acceptable surface active substance and provided that the indicated pharmaceutically acceptable surface active substance contains surface active substance with the value of hydrophilic-lipophilic balance (GLB) from 4 to 10.

31. Method according to claim 30, in which at least one indicated pharmaceutically acceptable water-soluble polymer has glass transition temperature Tg of at least 50 °C.

32. Method according to claim 30, in which at least one indicated pharmaceutically acceptable water soluble polymer contains the copolymer of N-vinylpyrrolidone and vinyl acetate and the specified surface active substance with the value of hydrophilic-lipophilic balance (GLB) from 4 to 10 is a mono composite ether of sorbitan fatty acid.

33. Method according to claim 30, in which at least one indicated pharmaceutically acceptable water soluble polymer contains the copovidone and the specified surface active substance with the value of hydrophilic-lipophilic balance (GLB) from 4 to 10 is a mono composite ether of sorbitan monolaurate."

The formula of the invention under the patent of Ukraine No. UA89220 is a multiclaim formula and it characterizes a group of inventions which share common invention idea.

According to the Article 5 of the Rules [3]:

"The application for an invention shall relate to a single or group of inventions which share common invention idea. The requirement of unity of invention is considered to be ensured if:

...

- the application refers to a group of inventions which share common invention idea, namely:

- inventions, one of which is intended to produce (manufacture) an another one, for example, device, substance or strain and the way of its production, manufacturing;

- inventions, one of which is intended for the implementation of the other one, for example, method and device for implementing the method;

- inventions, one of which is intended for the use of the other one (otherwise), for example, the method and the substance that is intended for use in the method;

- inventions of the same purpose, which provide the same technical result by fundamentally the same way (options)."

According to the Article 6.3.2.2. of the Rules [3]: *"Multiclaim formula that characterizes a group of inventions, has several independent claims. Each of them characterizes one of the inventions of the group. While each of the inventions of the group can be characterized using the dependent claims, subordinated to the appropriate independent claim".*

Group of inventions under patent of Ukraine No. UA89220 describes three objects:

a. ***HIV/AIDS treatment***, *which is characterized by independent claim 1 of the invention formula, and depending claims 2-24 of the invention formula;*

b. ***HIV/AIDS treatment***, *which is characterized by independent claim 25 of the invention formula, and depending claim 26 of the invention formula;*

c. ***HIV/AIDS treatment***, *which is characterized by independent claim 27 of the invention formula, and depending claims 28-33 of the invention formula.*

In this case, in accordance with Part 5 of Article 6 of the Law [1] the interpretation of the formula should be carried out within the description of the invention and appropriate drawings. Therefore, application materials and description of the invention should contain not only a reference to the purpose of the claimed object of invention (for new chemicals - its possible use), but also a description of the means and methods by which the invention is possible in the way as it is described in each Article of the claim and proof of such implementation. That is, the description of the invention must contain (within the scope of knowledge of an ordinary professional) the confirmation of actualization of the characteristics set in the invention formula.

II. ***Methodological framework research***

In the process of conducting the research and providing answers to the questions posed before the research it is necessary to take into account the provisions of Article 7 of the Law [1]:

«1. The invention meets the patentability requirement if it is new and if it has an inventive step and is industrially applicable.

<…>

3. An invention (utility model) is considered to be novel if it is not a part of technical level. For novelty evaluation the objects that are part of the technical level should be considered only separately.

4. The prior art of the invention includes all of the information that became available worldwide prior to the date of submission of the application to the Agency, or, if priority has been claimed, prior to the priority date.

5. The prior art of the invention also includes the contents of any application for a patent in Ukraine (including international applications, where Ukraine is claimed) in the version in which this application was filed first, provided that the date of its filing (and if the priority was claimed, the priority date) precedes the date, indicated in Part 4 of this Article, and that it was published on that date or thereafter.

<…>

7. The invention has an inventive level if it is not obvious for an expert, e.g. it does not clearly follow out of the prior art of the invention. When assessing inventive level, the content applications referred to in Part five of this Article, is not taken into account.

8. The invention (utility model) is considered to be industrially suitable, if it can be used in the industry or in another field of activity."

The Law of Ukraine [1] doesn't narrow the content of "expert" concept to "expert in the field of invention" concept. Therefore, in the process of inventive level study of claimed invention all of the knowledge, open for public use prior to priority date and that are related to any of the branches of science and technology, may be used.

For the purposes of research and explanation of some legally significant concepts, the specialist provides with the guidelines for substantial examination. Thus, the guidelines for examination in the European Patent Office (hereinafter referred to as the Guidelines) chapter I [7] contains:

«*4.1 General observations*

The application must disclose the invention in a clear and complete way, sufficient for the specialist in the field of invention to implement it.

"The specialist in the field of invention" is a practitioner who is knowledgeable not only in the theory of the field of application and references contained therein, but also in the general level of knowledge, which is known at the filing date.

Information on the subject contained in basic material references, monographs and textbooks is considered to be "general special knowledge".

Also chapter IV says:

«11.3 Expert in invention

"Expert in the field of invention" is a practicing professional in relevant field, who has average knowledge and skills and has the sum total of knowledge in the field of invention at some point ...

It is believed that he had access to everything that relates to the "prior art of the invention", in particular to the documents referred to in the search report, and that he had the normal means and capacity for routine work and experimentation. If the problem causes a specialist to seek a solution in another field of invention, the specialist in that field is an expert needed to solve the problem.

It is necessary also to take into account the fact that the specialist has the same level of knowledge for assessing inventive level and sufficient disclosure."

Thus, the information contained in the prior art of the invention refers to the common specialized knowledge.

Thus, the "expert" is the person who has knowledge in the relevant field, based on the information that became available to the public prior to the date of priority, and in its absence, to the date of application submitting and is contained in the manuals, reference books, monographs, textbooks in this field (prior art of the invention). The source of such information (prior art of the invention) may also lie in specifications to patents for inventions (utility models), or scientific publications, if the invention belongs to a field of research which is so new that relevant knowledge is still not available from other sources [6].

The obvious (the ones that clearly derive from the prior art of the invention) are those solutions that are obtained by conventional engineering based on well-known tools and methods that give the common result [4].

As for obviousness, this concept is also explained in the Guidelines [7], chapter IV mentioned above:

«11.4 Obviousness

Thus, in consideration of any formula defining the invention there is a question whether the expert in the relevant field on the basis of prior art of the invention for the date prior to application submission or priority date could derive in an obvious way something that is beyond the scope of the claimed formula. In this case the formula is not valid due to lack of an inventive level. The term "obvious" covers everything that does not go beyond the normal progress on techniques but merely follows clearly or logically from the prior art of the invention, it is something that does not require the implementation of any skill or ability beyond those expected from an expert. When checking for inventive level, as opposed to novelty (see IV, 9.3), it is permissible to interpret the published document in the light of the knowledge available not later than the day preceding the date of application submitting or priority date, valid for the claimed invention, and knowledge generally available for the expert not later than that day.

According to the Article 6.5.2.4. of the Rules [2]: *" For determination of novelty the objects that have become known prior to the date of application submission (or, if the priority has been claimed, prior to the date of priority), should be considered only separately. Information about the object can be given both in one, and in several sources of information."*

According to the Article 6.5.2.3. of the Rules [2]: *"Verification of the novelty is being done as to the whole totality of characteristics listed in the formula of the invention".*

According to the Article 6.5.4.2. of the Rules of consideration [2]:

"If the group of inventions is claimed, then the compliance test as to conditions of patentability is being held separately for each invention of the group. A group of inventions is recognized as thereof that meets the requirement of patentability if all the inventions of the group correspond to the conditions of patentability."

According to the Article 26.3. of the Guidelines [6]:

"A group of inventions is recognized as thereof that meets the determined requirement if all the inventions of the group correspond to these requirement ."

Invention is considered to correspond to the inventive level, if the solutions with the characteristics that coincide with the distinctive characteristics of claimed invention are unrevealed or, if such solutions were revealed and the publicity of the distinctive characteristics influence of the invention claimed for technical result indicated by the applicant is not confirmed.

According to the Article 6.5.3. of the Rules of consideration [2]:

"The invention has an inventive level if it is not obvious for an expert, e.g. it does not clearly follow out of the prior art of the invention. When determining the inventive level of the invention claimed the invention is compared not only with individual documents or their parts, but also with a combination of documents or their parts (so-called collective prototype), when the possibility of combining the documents or their parts is evident for the specialist.

<...>

6.5.3.2. When checking the inventive level the publicity of the prior art of the invention influence of the totality of claimed invention characteristics for achievement

of technical result stated by the applicant is being set. If such publicity is not set, then the invention is considered to meet the requirement of inventive level.

<...>

6.5.3.5. *The claimed invention is generally recognised as the one that does not meet the condition of inventive level if it is based on:*

addition of the known method by known part (parts), which is (are) added to it under known rules, to achieve a technical result, as to which the impact of such additions is determined;

replacement of any part (parts) of a known method by another known part (parts) to achieve a technical result, as to which the impact such replacement is determined;

the extraction of any method (element, action) with simultaneous extraction of the function which is conditioned upon its presence and accomplishment of the usual technical result for such extraction (simplification, reduction of mass, size, material, improvement of reliability, reducing of the process duration, etc);

enlargement of the number of similar elements or actions to enhance the technical result which is conditioned upon the presence of such elements or actions in the method;

implementation of known method or its part (part) from known material for achievement of technical result which is conditioned by known properties of this material;

creation of method which consists of known parts, the choice of which and the relationship between which is carried out by known rules, recommendations, and technical result, achieved in this case is conditioned by known properties of this material;

the application of previously known product (device, substance, a microorganism strain, etc.) or use of known method for new intended use, if a new intended use is conditioned by its known properties, structure, implementation and it is known that such properties, structure, implementation are needed for realization of said intended use;

change of quantitative characteristic (characteristics), showing of such characteristics in relationship or change of type, provided that the fact of the influence of each of the characteristics on indicated technical result is known and the new values of these characteristics or their relationships could be obtained, based on known dependency, consistencies".

According to the Article 25.2.2. of the Guidelines [6]:

"Checking of the inventive level is performed as to the totality of essential characteristics described in the independent claim of invention formula, by comparing this totality of characteristics with the obtained ones in a result of information search about the objects that are part of prior art of the invention."

According to the Article 25.5.2 of the Guidelines [6]:

"If an invention under an independent claim will be recognized as the one having no inventive level, the invention in general will be recognized as the one that has no inventive level".

Test for the inventive level is held for the invention, which is described in the independent claim of the formula. This test includes:

- identification of the most similar analogue;
- detection of the characteristics that distinguish the claimed invention from the most similar analogue, i.e. distinctive characteristics;
- selection of such solutions within the prior art of the invention that have the characteristics that coincide with the distinctive characteristics of the invention claimed.

Thus, to answer the question posed it is necessary to check each of the three objects of the group of inventions under the patent of Ukraine No. UA89220 concerning its compliance with the requirement of patentability.

Claim 6.5.2. of the Rules of consideration [2] contains the clarifications as to some of the documents that make up the prior art of the invention:

The prior art of the invention includes all of the information that became available worldwide prior to the date of submission of the application to the State Agency, or, if priority has been claimed, prior to the priority date.

<...>

The prior art of the invention also includes the contents of any application for a patent in Ukraine (including international applications, where Ukraine is claimed) in the version in which this application was filed first, provided that the date of its filing (and if the priority was claimed, the priority date) precedes the date of submission of the application to the State Agency, or, if priority has been claimed, prior to the priority date, and that it was published on that date or thereafter.

The content of the application in the version in which this application was initially submitted is determined by the content of the documents of the application submitted to the State Agency on the date of submitting, and if the application has priority than it is determined by its content, which coincides with the content of the materials which were the basis for granting of the right of priority.

If the earlier application is withdrawn or is considered to be withdrawn before its publication, however, the publication of information about this application took place as the preparation for it had been conducted, the content of such application is not included to the prior art of the invention".

In this case, in accordance with the Article 6.5.2.1 of the Rules of consideration [2] the date, which determines the inclusion of information sources to the prior art of the invention is:

for the published descriptions of security documents - the publishing date indicated therein;

for the published information about an application for patent for invention submitted to the State Agency - the publishing date indicated therein;

for printed publications - the date of release, and if it is impossible to determine the date of release, then the last day of the month or December 31 of the year indicated in the publication if the date of release is defined by a month or a year only;

for deposited manuscripts, articles, reviews, monographs, etc. - the date of their deposit;

for reports on research works, explanatory notes to the research and development works or other engineering drawings, technological and design documentation, which is available in the bodies of scientific and technical information - the date of its entry to these bodies;

for normative-technical documentation - the date of its registration in competent bodies;

for materials of dissertations and dissertations theses, published as manuscript - the date of entry to the library;

for the competition works - the date of displaying them for review, confirmed by the documents relating to the competition;

for information sources that are perceived visually (posters, models, products, etc.), - documentally confirmed date, from which the review of such information became possible;

for exhibits placed at the exhibitions - documentally confirmed date of the beginning of its demonstration;

for oral presentations, lectures, speeches, etc. - date of presentation, lecture, speech, if they were fixed by sound recording equipment or stenography according to the prescribed procedure effective for the current date;

for information about the technical methods, which became known as a result of their use - documentally confirmed date, from which this information became available to the public;

for radio, television, or cinema messages - the date of such message, if it is registered on the appropriate data storage device according to the prescribed procedure effective for the current date.

To answer the question posed the sources that compose the prior art of the invention (the documents that became known prior to the priority date) of the patent of Ukraine for invention No. UA89220 are provided for research.

The below Table 1 provides a list of sources relating to the objects of the invention for a patent of Ukraine for invention No. UA89220.

A list of relevant documents pertaining to the case, and the analysis of which is to be conducted to answer questions posed (Source 1-4).

Table 1

Number	Document	Publication date
D1	WO 01/34119	17.05.2001
D2	WO 2005/039551 (similar to UA85564)	06.05.2005 This international application (WO 2005/039551), published after the priority date of the patent of Ukraine for invention No. UA89220, but has the earlier priority (28.08.2003) than the date when the patent of Ukraine for invention No. UA89220, has

Number	Document	Publication date
		entered to the national phase in Ukraine in accordance with Part 5, Para. 7 of the Law [1] and it is a document of the prior art of the invention, which can be countered by novelty according to Part 5, Para. 7 of the Law [1]
D3	Approved labeling "KALETRA"	15.09.2000
D4	"KALETRA"	25.10.2005

The Source D4 is used in a study only for reference and explanation and is not a basis for conclusions made.

According to the Article 11.5.1 of the Guideline [7], chapter IV:

"The closest prior art of the invention is the one that, by a single reference, discloses a combination of features which is the starting point, the most success promising for the apparent development, leading to the invention. In selecting the closest prior art of the invention first of all it is necessary to think about the fact that it must be aimed at a similar purpose or effect as the invention or at least must belong to the same or a closely related technical field as the claimed invention. Practically the closest prior art of the invention is the one that corresponds to a similar use and requires the minimum of structural and functional modifications to obtain the claimed invention."

The provided for research documents are the sources that make up the prior art of the invention for the tested invention No. UA89220.

III. Patentability conditions research "novelty" and "inventive level"

According to the Methodological provisions of the source [6] checking novelty is made as to the entire list of identifiable characteristics given in an independent formula claim of the invention, by comparing the list of characteristics with the information about the objects that are part of the prior art of the invention, in a tested case, with information about the objects contained in the Sources 1-4.

Source D1 *contains the following information:*

- (page 33, lines 4-17):

"20. A method of treating an HIV infection comprising administering an effective amount of a solid dispersion of Claim 1 to a mammal in need of such treatment, wherein said pharmaceutical compound is an HIV protease inhibitor.

21. The method of Claim 20 wherein said HIV protease inhibitor is selected from the group consisting of (2S,3S,5S)-5-(N-(N-((N-methyl-N-((2-isopropyl-4-thiazolyl)methyl)amino)carbonyl)L-valinyl)amino-2-(N-((5- thiazolyl)methoxy-carbonyl)-amino)-amino-1,6-diphenyl-3- hydroxyhexane (ritonavir) and (2S, 3S, 5S)-2-(2,6)- Dimethylphenoxyacetyl)amino-3-hydroxy-5-

[2S-(l-tetrahydro-pyrimid-2-onyl)-3-methyl butanol] amino-1,6-diphenylhexane (ABT-378).”

- (page 29, lines 3-7):

“1. A pharmaceutical composition comprising a solid dispersion of a pharmaceutical compound, a water soluble carrier, and a crystallization inhibitor selected from the group consisting of polyvinylpyrrolidone (PVP) and hydroxypropylcellulose (HPMC).”

- (page 10, line 20 - page 11, line 6):

“In the instant invention, PEG 8000 is used as the hydrophilic matrix. Also employed in this formulation is polyvinylpyrrolidone (PVP), which is an example of a hydrophilic, amorphous polymer, and is used to inhibit crystallization. Other hydrophilic, amorphous polymers include hydroxypropylmethylcellulose (HPMC), or other pharmaceutically acceptable hydrophilic, amorphous polymers. Specifically, PVP PF 17 is used within the PEG matrix to inhibit the crystallization of the drug of interest. A range of l%-95% (w/w) of PVP can be employed, with a range of 1%-15% (w/w) being preferred.”

- (page 11, lines 16-18):

“ dissolution. PVP has the added advantage of having a high Tg, which imparts stabilization of amorphous regions by reducing mobility. Therefore, this invention affords the”

- (page 14, lines 10-12):

“protease inhibitor. An example of an HIV protease inhibitor is ABT-538 (ritonavir), the chemical structure of which is represented herein below as a compound of formula I”

- (page 15, line 8 - page 16, line 4):

“Additional HIV protease inhibitors which may be formulated into a solid dispersion of the instant invention include compounds of formula II.

A compound of formula II is known as ABT-3 78 ((2S,3S,5S)-2-(2,6-dimethylphenoxyacetyl)-amino-3-hydroxy-5-(2S-(l-tetrahydropyrimid-2-onyl)-3-methyl-butanoyl)amino-1,6-diphenylhexane). This and other”

- (page 30, line 23 - page 31, line 2):

“10. The composition of Claim 1 further comprising an additive or a mixture of additives of additives independently selected from the group consisting of pharmaceutically acceptable surfactants and antioxidants”

Next is the translation of above mentioned information:

- (page 33, lines 4-17):

«*20. A method of treating an HIV infection comprising administering an effective amount of a solid dispersion of Claim 1 to a mammal in need of such treatment, wherein said pharmaceutical compound is an HIV protease inhibitor.*

The method of Claim 20 wherein said HIV protease inhibitor is selected from the group consisting of (2S,3S,5S)-5-(N-(N-((N-methyl-N-((2-isopropyl-4-thiazolyl)methyl)amino)carbonyl)L-valinyl)amino-2-(N-((5- thiazolyl)methoxy-carbonyl)-amino)-amino-1,6-diphenyl-3- hydroxyhexane (ritonavir) and (2S, 3S, 5S)-2-(2,6)- Dimethylphenoxyacetyl)amino-3-hydroxy-5-

[2S-(l-tetrahydro-pyrimid-2-onyl)-3-methyl butanol] amino-1,6-diphenylhexane (ABT-378).”

- (page 29, lines 3-7):

«1. A pharmaceutical composition comprising a solid dispersion of a pharmaceutical compound, a water soluble carrier, and a crystallization inhibitor selected from the group consisting of polyvinylpyrrolidone (PVP) and hydroxypropylcellulose (HPMC).

- (page 10, line 20 - page 11, line 6):

" In the instant invention, PEG 8000 is used as the hydrophilic matrix. Also employed in this formulation is polyvinylpyrrolidone (PVP), which is an example of a hydrophilic, amorphous polymer, and is used to inhibit crystallization. Other hydrophilic, amorphous polymers include hydroxypropylmethylcellulose (HPMC), or other pharmaceutically acceptable hydrophilic, amorphous polymers. Specifically, PVP PF 17 is used within the PEG matrix to inhibit the crystallization of the drug of interest. A range of l%-95% (w/w) of PVP can be employed, with a range of 1%-15% (w/w) being preferred."

- (page 11, lines 16-18):

«… dissolution. PVP has the added advantage of having a high Tg, which imparts stabilization of amorphous regions by reducing mobility. Therefore, this invention affords the. ...»

- (page 14, lines 10-12):

«… An example of an HIV protease inhibitor is ABT-538 (ritonavir), the chemical structure of which is represented herein below as a compound of formula I..."

- (page 15, line 8 - page 16, line 4):

« Additional HIV protease inhibitors which may be formulated into a solid dispersion of the instant invention include compounds of formula II.

A compound of formula II is known as ABT-3 78 ((2S,3S,5S)-2-(2,6-dimethylphenoxyacetyl)-amino-3-hydroxy-5-(2S-(l-tetrahydropyrimid-2-onyl)-3-methyl-butanoyl)amino-1,6-diphenylhexane).. …”

- (page 30, line 23 - page 31, line 2):

«10. The composition of Claim 1 further comprising an additive or a mixture of additives of additives independently selected from the group consisting of pharmaceutically acceptable surfactants and antioxidants.”

*That is, Source **D1** contains the description of HIV treatment, which includes introduction of solid dispersion containing lopinavir (((2S,3S,5S)-2-(2,6-dimetyl phenoxyacetyl)amino-3-hydroxy-5-(2S-(1-tetrahydropyrimidin-2-onil)-3-metylbutanoil)amino-1,6-diphenylhexane)) and ritonavir ((2S,3S,5S)-5-(N-(N-((N-methyl-N-((2-isopropyl-4-thiazolyl)methyl)amino)carbonyl)L-valinil)amino-2-(N -((5-thiazolyl) methoxy-carbonyl)amino)amino-1,6-diphenyl-3-hydroxy hexane); a pharmaceutically acceptable water-soluble polymer with a high glass transition temperature Tg (polyvinyl pyrrolidone) and a pharmaceutically acceptable surface-active agent. Also there is the way to treat HIV, which includes the introduction of solid dosage form to patients who need such treatment, provided that the specified dosed form contains lopinavir. However, the source **D1** doesn’t contain any*

instructions on the use of medicinal product - after meals or under fasting condition and there is no information on hydrophilic-lipophilic balance (GLB) of the surface active substance used.

***Source D2** contains the following information:*

- (page 1, lines 5-6):

"The present invention is directed to a solid pharmaceutical dosage form comprising at least one HIV protease inhibitor, and a process for preparing same."

- (page 2, lines 17-21):

"The present invention provides a solid pharmaceutical dosage form comprising a solid dispersion of at least one HIV protease inhibitor in at least one pharmaceutically acceptable water-soluble polymer and at least one pharmaceutically acceptable surfactant. In one embodiment, the pharmaceutically acceptable water-soluble polymer has a glass transition temperature (Tg) of at least about 50 °C."

- (page 2, line 23 - page 3, line 5):

"The term "solid dispersion" defines a system in a solid state (as opposed to a liquid or gaseous state) comprising at least two components, wherein one component is dispersed evenly throughout the other component or components. For example, the active ingredient or combination of active ingredients is dispersed in a matrix comprised of the pharmaceutically acceptable water-soluble polymer(s) and pharmaceutically acceptable surfactant(s). The term "solid dispersion" encompasses systems having small particles, typically of less than 1 |im in diameter, of one phase dispersed in another phase. When said dispersion of the components is such that the system is chemically and physically uniform or homogenous throughout or consists of one phase (as defined in thermodynamics), such a solid dispersion will be called a "solid solution" or a "glassy solution". A glassy solution is a homogeneous, glassy system in which a solute is dissolved in a glassy solvent. Glassy solutions and solid solutions of HIV protease inhibitors are preferred physical systems. These systems do not contain any significant amounts of active ingredients in their crystalline or microcrystalline state, as evidenced by thermal analysis (DSC) or X-ray diffraction analysis (WAXS)."

- (page 5, lines 12-17):

"In still another embodiment, the present invention provides a dosage form wherein said HIV protease inhibitor is a combination of ritonavir and lopinavir, the dosage form showing a dose-adjusted AUC of ritonavir plasma concentration in dogs of at least about 9 µg.h/ml/100 mg and a dose-adjusted AUC of lopinavir plasma concentration of at least about 20 µg.h/ml/100 mg (preferably at least about 22.5 µg.h/ml/100 mg, most preferred at least about 35 µ.h/ml/100 mg)."

- (page 6, lines 9-17):

"The term "pharmaceutically acceptable surfactant" as used herein refers to a pharmaceutically acceptable non-ionic surfactant. In one embodiment, the dosage form is comprising at least one surfactant having an hydrophilic lipophilic balance (HLB) value of from about 4 to about 10, preferably from about 7 to about 9. The HLB system (Fiedler, H.B., Encyclopedia of Excipients, 5th ed., Aulendorf: ECV-Editio-Cantor-Verlag (2002)) attributes numeric values to surfactants, with lipophilic

substances receiving lower HLB values und hydrophilic substances receiving higher HLB values. Surfactants having an HLB value of from about 4 to about 10 suitable for use in the present invention include for example, but are not limited thereto:"

- (page 7, lines 12-28):

"Besides the surfactant having an HLB value of from about 4 to about 10, the dosage form may comprise additional pharmaceutically acceptable surfactants such as polyoxyethylene castor oil derivates, e.g. polyoxyethyleneglycerol triricinoleate or polyoxyl 35 castor oil (Cremophor® EL; BASF Corp.) or polyoxyethyleneglycerol oxystearate such as polyethylenglycol 40 hydrogenated castor oil (Cremophor® RH 40) or polyethylenglycol 60 hydrogenated castor oil (Cremophor® RH 60); or block copolymers of ethylene oxide and propylene oxide, also known as polyoxyethylene polyoxypropylene block copolymers or polyoxyethylene polypropyleneglycol, such as Poloxamer® 124, Poloxamer® 188, Poloxamer® 237, Poloxamer® 388, Poloxamer® 407 (BASF Wyandotte Corp.); or a mono fatty acid ester of polyoxyethylene (20) sorbitan, e.g. polyoxyethylene (20) sorbitan monooleate (Tween® 80), polyoxyethylene (20) sorbitan monostearate (Tween® 60), polyoxyethylene (20) sorbitan monopalmitate (Tween® 40), polyoxyethylene (20) sorbitan monolaurate (Tween® 20).

Where such additional surfactants are used, the surfactant having an HLB value of from about 4 to about 10 generally accounts for at least about 50 % by weight, preferably at least about 60 % by weight, of the total amount of surfactant used."

- (page 7, line 30 - page 8, line 8):

"The water-soluble polymer employed in the present investment has a Tg of at least about $50\ ^{0}$ C, preferably at least about $60\ ^{0}$ C, most preferred from about $180\ ^{0}$ C. Methods for determining Tg values of the organic polymers are described in "Introduction to Physical Polymer Science", 2nd Edition by L.H. Sperling, published by John Wiley & Sons, Inc., 1992. The Tg value can be calculated as the weighted sum of the Tg values for homopolymers derived from each of the individual monomers, i.e., that make up the polymer: $Tg = \Sigma\ W_i\ X_i$ where W is the weight percent of monomer in the organic polymer, and X is the Tg value for the homopolymer derived from monomer i. Tg values for the homopolymers may be taken from "Polymer Handbook", 2nd Edition by J. Brandrup and E.H. Immergut, Editors, published by John Wiley & Sons, Inc., 1975."

- (page 20, formula claims Nos.1-5):

"1. A solid pharmaceutical dosage form which comprises a solid dispersion of at least one HIV protease inhibitor and at least one pharmaceutically acceptable water-soluble polymer and at least one pharmaceutically acceptable surfactant, said pharmaceutically acceptable water-soluble polymer having a Tg of at least about 50 °C.

2. The dosage form of claim 1 comprising a glassy solution or solid solution of said HIV protease inhibitor.

3. The dosage form of claim 1, wherein said pharmaceutically acceptable surfactant has an HLB value of from about 4 to about 10.

4. The dosage form of claim 1, wherein said pharmaceutically acceptable surfactant is a combination of at least one pharmaceutically acceptable surfactant having an HLB value of from about 4 to about10 and at least one further pharmaceutically acceptable surfactant.

5. The dosage form of Claim 1 wherein said pharmaceutically acceptable surfactant is a sorbitan fatty acid ester."

- (page 22, formula claim No. 12):

" 12. The dosage form of claim 1 wherein said HIV protease inhibitor is a combination of (2S,3S,5S)-5-(N-(N-((N-methyl-N-((2-isopropyl-4-thiazolyl)methyl)amino)carbonyl)- L-valinyl)amino-2-(N-((5-thiazolyl)methoxy-carbonyl)-amino)-amino-l,6-diphenyl-3- hydroxyhexane (ritonavir) and (2S,3S,5S)-2-(2,6-Dimethylphenoxyacetyl)amino-3- hydroxy-5-[2S-(l-tetrahydropyrimid-2-onyl)-3-methylbutanoyl] amino-1,6- diphenylhexane (lopinavir)."

- (page 22, formula claims Nos.14-16):

"14.The solid dosage form of Claim 1 wherein said water-soluble polymer has a Tg of from about 80 to about 180 °C.

15 The solid dosage form of Claim -1 wherein said water-soluble polymer is a homopolymer or copolymer of N-vinylpyrrolidone.

16 The solid dosage form of Claim 1 wherein said water-soluble polymer is a copolymer of N-vinylpyrrolidone and vinyl acetate."

- (page 23, formula claim No. 26):

"24. A solid pharmaceutical, dosage form comprising,
(2S,3S,5S)-2-(2,6-Dimethylphenoxyacetyl)amino-3-hydroxy-5-[2S-(l-tetrahydro-pyrimid-2-onyl)-3-methylbutanoyl]amino-1,6-diphenylhexane (lopinavir);
a copolymer of N-vinylpyrrolidone; and
a sorbitan fatty acid ester."

- (page 24, formula claim No. 26):

"26. A solid pharmaceutical dosage form comprising,
(2S,3S,5S)-5-(N-(N-((N-methyl-N-((2-isopropyl-4-thiazolyl)methyl)amino)carbonyl)-L-valinyl)amino-2-(N-((5-thiazolyl)methoxy-carbonyl)-amino)-amino-l,6-diphenyl-3-hydroxyhexane (ritonavir) and (2S,3S,5S)-2-(2,6-Dimethylphenoxyacetyl)amino-3-hydroxy- 5-[2S-(l-tetrahydro-pyrimid-2-onyl)-3-methylbutanoyl]amino-l,6-diphenylhexane (lopinavir);
a copolymer of N-vinylpyrrolidone and vinyl acetate; and
a sorbitan fatty acid ester."

- (page 25, formula claim No. 37):

"37. A method of treating an HIV infection comprising administering the solid dosage form of any of claim 22-36 to a mammal in need of such treatment."

Next is the translation of above mentioned information:

- (page 1, lines 5-6 (while quoting the translation of Source **D2** was used in the edition of its analogue UA85564)):

" The present invention is directed to a solid pharmaceutical dosage form comprising at least one HIV protease inhibitor, and a process for preparing same."

- (page 2, lines 17-21 (while quoting the translation of Source **D2** was used in the edition of its analogue UA85564)):

" The present invention provides a solid pharmaceutical dosage form comprising a solid dispersion of at least one HIV protease inhibitor in at least one pharmaceutically acceptable water-soluble polymer and at least one pharmaceutically acceptable surfactant. In one embodiment, the pharmaceutically acceptable water-soluble polymer has a glass transition temperature (Tg) of at least about 50 °C.

- (page 2, line 23 - page 3, line 5 (while quoting the translation of Source **D2** was used in the edition of its analogue UA85564)):

" The term "solid dispersion" defines a system in a solid state (as opposed to a liquid or gaseous state) comprising at least two components, wherein one component is dispersed evenly throughout the other component or components. For example, the active ingredient or combination of active ingredients is dispersed in a matrix comprised of the pharmaceutically acceptable water-soluble polymer(s) and pharmaceutically acceptable surfactant(s). The term "solid dispersion" encompasses systems having small particles, typically of less than 1 |im in diameter, of one phase dispersed in another phase. When said dispersion of the components is such that the system is chemically and physically uniform or homogenous throughout or consists of one phase (as defined in thermodynamics), such a solid dispersion will be called a "solid solution" or a "glassy solution". A glassy solution is a homogeneous, glassy system in which a solute is dissolved in a glassy solvent. Glassy solutions and solid solutions of HIV protease inhibitors are preferred physical systems. These systems do not contain any significant amounts of active ingredients in their crystalline or microcrystalline state, as evidenced by thermal analysis (DSC) or X-ray diffraction analysis (WAXS)."

- (page 5, lines 12-17 (while quoting the translation of Source **D2** was used in the edition of its analogue UA85564)):

" In still another embodiment, the present invention provides a dosage form wherein said HIV protease inhibitor is a combination of ritonavir and lopinavir, the dosage form showing a dose-adjusted AUC of ritonavir plasma concentration in dogs of at least about 9 µg.h/ml/100 mg and a dose-adjusted AUC of lopinavir plasma concentration of at least about 20 µg.h/ml/100 mg (preferably at least about 22.5 µg.h/ml/100 mg, most preferred at least about 35 µ.h/ml/100 mg)".

- (page 6, lines 9-17 (while quoting the translation of Source **D2** was used in the edition of its analogue UA85564)):

" The term "pharmaceutically acceptable surfactant" as used herein refers to a pharmaceutically acceptable non-ionic surfactant. In one embodiment, the dosage form is comprising at least one surfactant having an hydrophilic lipophilic balance (HLB) value of from about 4 to about 10, preferably from about 7 to about 9. The HLB system (Fiedler, H.B., Encyclopedia of Excipients, 5th ed., Aulendorf: ECV-Editio-Cantor-Verlag (2002)) attributes numeric values to surfactants, with lipophilic substances receiving lower HLB values und hydrophilic substances receiving higher HLB values. Surfactants having an HLB value of from about 4 to about 10 suitable for use in the present invention include for example, but are not limited thereto:"

- (page 7, lines 12-28 (while quoting the translation of Source **D2** was used in the edition of its analogue UA85564)):

"Besides the surfactant having an HLB value of from about 4 to about 10, the dosage form may comprise additional pharmaceutically acceptable surfactants such as polyoxyethylene castor oil derivates, e.g. polyoxyethyleneglycerol triricinoleate or polyoxyl 35 castor oil (Cremophor® EL; BASF Corp.) or polyoxyethyleneglycerol oxystearate such as polyethylenglycol 40 hydrogenated castor oil (Cremophor® RH 40) or polyethylenglycol 60 hydrogenated castor oil (Cremophor® RH 60); or block copolymers of ethylene oxide and propylene oxide, also known as polyoxyethylene polyoxypropylene block copolymers or polyoxyethylene polypropyleneglycol, such as Poloxamer® 124, Poloxamer® 188, Poloxamer® 237, Poloxamer® 388, Poloxamer® 407 (BASF Wyandotte Corp.); or a mono fatty acid ester of polyoxyethylene (20) sorbitan, e.g. polyoxyethylene (20) sorbitan monooleate (Tween® 80), polyoxyethylene (20) sorbitan monostearate (Tween® 60), polyoxyethylene (20) sorbitan monopalmitate (Tween® 40), polyoxyethylene (20) sorbitan monolaurate (Tween® 20).

Where such additional surfactants are used, the surfactant having an HLB value of from about 4 to about 10 generally accounts for at least about 50 % by weight, preferably at least about 60 % by weight, of the total amount of surfactant used."

- (page 7, line 30 - page 8, line 8 (while quoting the translation of Source **D2** was used in the edition of its analogue UA85564)):

"The water-soluble polymer employed in the present investment has a Tg of at least about 50 0 C, preferably at least about 60 0 C, most preferred from about 180 0 C. Methods for determining Tg values of the organic polymers are described in "Introduction to Physical Polymer Science", 2nd Edition by L.H. Sperling, published by John Wiley & Sons, Inc., 1992. The Tg value can be calculated as the weighted sum of the Tg values for homopolymers derived from each of the individual monomers, i.e., that make up the polymer: Tg = Σ Wi Xi where W is the weight percent of monomer in the organic polymer, and X is the Tg value for the homopolymer derived from monomer i. Tg values for the homopolymers may be taken from "Polymer Handbook", 2nd Edition by J. Brandrup and E.H. Immergut, Editors, published by John Wiley & Sons, Inc., 1975."

- (page 20, formula claims Nos.1-5):

"1. A solid pharmaceutical dosage form which comprises a solid dispersion of at least one HIV protease inhibitor and at least one pharmaceutically acceptable water-soluble polymer and at least one pharmaceutically acceptable surfactant, said pharmaceutically acceptable water-soluble polymer having a Tg of at least about 50 °C.

2. The dosage form of claim 1 comprising a glassy solution or solid solution of said HIV protease inhibitor.

3. The dosage form of claim 1, wherein said pharmaceutically acceptable surfactant has an HLB value of from about 4 to about 10.

4. The dosage form of claim 1, wherein said pharmaceutically acceptable surfactant is a combination of at least one pharmaceutically acceptable surfactant

having an HLB value of from about 4 to about10 and at least one further pharmaceutically acceptable surfactant.

5. The dosage form of Claim 1 wherein said pharmaceutically acceptable surfactant is a sorbitan fatty acid ester."

- (page 22, formula claim No. 12):

" 12. The dosage form of claim 1 wherein said HIV protease inhibitor is a combination of (2S,3S,5S)-5-(N-(N-((N-methyl-N-((2-isopropyl-4-thiazolyl)methyl)amino)carbonyl)- L-valinyl)amino-2-(N-((5-thiazolyl)methoxy-carbonyl)-amino)-amino-l,6-diphenyl-3- hydroxyhexane (ritonavir) and (2S,3S,5S)-2-(2,6-Dimethylphenoxyacetyl)amino-3- hydroxy-5-[2S-(l-tetrahydropyrimid-2-onyl)-3-methylbutanoyl] amino-1,6- diphenylhexane (lopinavir)."- (page 22, formula claims Nos.14-16):

"14.The solid dosage form of Claim 1 wherein said water-soluble polymer has a Tg of from about 80 to about 180 °C.

15 The solid dosage form of Claim -1 wherein said water-soluble polymer is a homopolymer or copolymer of N-vinylpyrrolidone.

16 The solid dosage form of Claim 1 wherein said water-soluble polymer is a copolymer of N-vinylpyrrolidone and vinyl acetate."

- (page 23, formula claim No. 24):

"24. A solid pharmaceutical, dosage form comprising,

(2S,3S,5S)-2-(2,6-Dimethylphenoxyacetyl)amino-3-hydroxy-5-[2S-(l-tetrahydro-pyrimid-2-onyl)-3-methylbutanoyl]amino-1,6-diphenylhexane (lopinavir);

a copolymer of N-vinylpyrrolidone; and

a sorbitan fatty acid ester."

- (page 24, formula claim No. 26):

"26. A solid pharmaceutical dosage form comprising,

(2S,3S,5S)-5-(N-(N-((N-methyl-N-((2-isopropyl-4-thiazolyl)methyl)amino)carbonyl)-L-valinyl)amino-2-(N-((5-thiazolyl)methoxy-carbonyl)-amino)-amino-l,6-diphenyl-3-hydroxyhexane (ritonavir) and (2S,3S,5S)-2-(2,6-Dimethylphenoxyacetyl)amino-3-hydroxy- 5-[2S-(l-tetrahydro-pyrimid-2-onyl)-3-methylbutanoyl]amino-l,6-diphenylhexane (lopinavir);

a copolymer of N-vinylpyrrolidone and vinyl acetate; and

a sorbitan fatty acid ester."

- (page 25, formula claim No. 37):

"37. A method of treating an HIV infection comprising administering the solid dosage form of any of claim 22-36 to a mammal in need of such treatment."

That is, ***the Source 2*** *describes the way to treat HIV infection, which includes the introduction of solid dosage form to a mammal that needs such treatment, provided that the specified dosed form contains lopinavir or a combination of lopinavir and ritonavir, which are inhibitors of HIV protease, and which contains solid dispersion, or vitreous solution, or solid solution of lopinavir and ritonavir in a pharmaceutically acceptable water soluble polymer with glass transition temperature Tg at least 50 °C and which also contains a pharmaceutically acceptable surface active substance that has a value of hydrophilic-lipophilic balance (GLB) from 4 to 10. Copolymer of N-*

vinylpyrrolidone and vinyl acetate may be used as above mentioned acceptable water soluble polymer, and ether of sorbitan fatty acid may be used as surface active substance.

***Source D3** contains the following information:*

- (page 3, 2-3 paragraphs from the top):

"Lopinavir is a white to light tan powder. It is freely soluble in methanol and Ethanot, soluble in isopropanol and practically insoluble in water. KALETRA capsules are available for oral administration in a strength of 133.3 mg lopinavir and 33.3 mg ritonavir with the following inactive ingredients: FD&C Yellow No. 6, gelatin, glycerin, oleic acid, polyoxyl 35 castor oil, Propylene glycol, sorbitol special, titanium dioxide, and water."

- (page 20, 2 paragraphs from the top):

"KALETRA should be taken with food to enhance absorption."

8. *Next is the translation of above mentioned information:*

- (page 3, 2-3 paragraphs from the top):

"Lopinavir is a white to light tan powder. It is freely soluble in methanol and Ethanot, soluble in isopropanol and practically insoluble in water.

KALETRA capsules are available for oral administration in a strength of 133.3 mg lopinavir and 33.3 mg ritonavir with the following inactive ingredients: FD&C Yellow No. 6, gelatin, glycerin, oleic acid, polyoxyl 35 castor oil, Propylene glycol, sorbitol special, titanium dioxide, and water."

- (page 20, 2 paragraphs from the top):

"KALETRA should be taken with food to enhance absorption."

*Source **D3** shows that Lopinavir is practically insoluble in water and KALETRA capsules should be used with food necessarily.*

Thus, for the date of priority, according to the materials found in the process of patent search, the expert in the field of pharmaceuticals got to know the following:

a. *the description of HIV treatment, which includes introduction of solid dispersion containing lopinavir (((2S,3S,5S)-2-(2,6-dimetyl phenoxyacetyl)amino-3-hydroxy-5-(2S- (1-tetrahydropyrimidin-2-onil)-3-metylbutanoil)amino-1,6-diphenylhexane)) and/or ritonavir ((2S,3S,5S)-5-(N-(N-((N-methyl-N-((2-isopropyl-4-thiazolyl) methyl)amino)carbonyl)L-valinil)amino-2-(N-((5-thiazolyl)methoxy-carbonyl)amino)amino-1,6-diphenyl-3-hydroxy hexane); a pharmaceutically acceptable water-soluble polymer with a high glass transition temperature Tg (polyvinyl pyrrolidone) and a pharmaceutically acceptable surface-active agent **D1**.*

b. *Also there was the way to treat HIV, which includes the introduction of solid dosage form to patients who need such treatment, provided that the specified dosed form contains lopinavir **D1**, which is practically insoluble in water **D3**;*

c. *also the Source **D2** describes the way to treat HIV infection, which includes the introduction of solid pharmaceutical dosage form to a mammal that needs such treatment, provided that the specified dosed form contains lopinavir or a combination of lopinavir and ritonavir, which are inhibitors of HIV protease, and which contains solid dispersion, or vitreous solution, or solid solution of lopinavir and ritonavir in a pharmaceutically acceptable water soluble polymer with glass transition*

temperature Tg at least 50 °C and which also contains a pharmaceutically acceptable surface active substance that has a value of hydrophilic-lipophilic balance (GLB) from 4 to 10. Copolymer of N-vinylpyrrolidone and vinyl acetate may be used as above mentioned acceptable water soluble polymer, and ether of sorbitan fatty acid may be used as surface active substance.

*So, the Source **D2** describes the way to treat HIV/AIDs infection, which includes the introduction of solid pharmaceutical dosage form to a person that needs such treatment, provided that the specified dosed form contains lopinavir or a combination of lopinavir and ritonavir in the form of solid solution or solid dispersion; pharmaceutically acceptable water soluble polymer with glass transition temperature Tg at least 50 °C and which also contains a pharmaceutically acceptable surface active substance that has a value of hydrophilic-lipophilic balance (GLB) from 4 to 10.*

That is, the object of the invention under an independent claim 1 of the patent of Ukraine for invention No. UA89220 is a part of prior art of the invention and, therefore, does not meet the "novelty" requirement of patentability.

*The only difference of suggested method of HIV/AIDS treatment in the patent of Ukraine for invention No. UA89220 is the administration of the specified dosing form with no food or in conditions of fasting. At the same time Source **D2** doesn't provide any instructions as to administration schedule of the well-known solid pharmaceutical dosage form, which should be used after a meal (with food), or under fasting condition. It is confirmed by the description of the patent of Ukraine for invention No. UA89220 (column 36, 4th text paragraph from the top) "Dosed form of this invention shows no effect of food ", i.e., bioavailability of solid pharmaceutical dosage form used for the treatment of HIV/AIDS does not depend on administration schedule of dosage form - after meal (with food), or under fasting condition. This is also confirmed by an approved instruction (Source **D4**[1]) for tablets of medicinal product KALETRA, which had been approved after the priority date of the patent of Ukraine for invention No. UA89220, and the invention protected by this patent was the base of it "Cmax and AUC indicators did not show any significant clinical changes after administration of Kaletra tablets with food as compared with fast conditions administration" (the Source **D4**, page. 8, 5th text paragraph from the top), "Kaletra tablets can be used with or without food" (the Source **D4**, page. 28, 5th text paragraph from the top).*

That is, the characteristic of an independent claim 1 of the formula of invention No. UA89220 "the indicated dosage form is administered by a patient with no food or in fasting conditions" is irrelevant, since the achievement of technical result, namely, effective treatment of HIV/AIDS is possible regardless of the method of administration of the solid pharmaceutical dosage form and achievement of technical result is conditioned only by the features (significant characteristics) of solid pharmaceutical dosage form used in method of treatment .

According to the Article 6.6.1. of the Rules [3]: The essence of the invention (utility model) is a combination of fundamental features sufficient to achieve a technical result which provides the invention (utility model). In other words, the characteristics are substantial if they affect the technical result that can be achieved,

i.e. are in cause-and-effect relationship with the mentioned result." In the case of the totality of characteristics as for an independent claim 1 of the patent of Ukraine for invention No. UA89220 there is no cause-and-effect relationship between a use of solid pharmaceutical dosage form and technical result, namely, effective treatment of HIV/AIDs. Therefore, the characteristic of an independent claim 1 of formula invention No. UA89220 concerning the administration schedule of dosage form is not taken into account because it is irrelevant.

*Source **D2** also describes the way to treat HIV/AIDs infection, which includes the introduction of solid pharmaceutical dosage form to a person that needs such treatment, provided that the specified dosed form contains lopinavir or a combination of lopinavir and ritonavir in the form of solid solution or solid dispersion; pharmaceutically acceptable water soluble polymer with glass transition temperature Tg at least 50 °C and which also contains combinations of surface active substances that have a value of hydrophilic-lipophilic balance (GLB) from 4 to 10.*

*That is, **the object of the invention under an independent claim 25 of the patent of Ukraine for invention No. UA89220 is a part of prior artof the invention and, therefore, does not meet the "novelty" requirement of patentability.***

*In the same way as in formula claim 1 the only difference of suggested method of HIV/AIDS treatment in the patent of Ukraine for invention No. UA89220 as to independent claim 25 is the administration of the specified dosing form with no food or in conditions of fast. At the same time Source **D2** doesn't provide any instructions as to administration schedule of the well-known solid pharmaceutical dosage form, which should be used after a meal (with food), or under fasting condition. It is confirmed by the description of the patent of Ukraine for invention No. UA89220 (column 36, 4th text paragraph from the top) "Dosed form of this invention shows no effect of food ", i.e., bioavailability of solid pharmaceutical dosage form used for the treatment of HIV/AIDS does not depend on administration schedule of dosage form - after meal (with food), or under fasting condition. This is also confirmed by an approved instruction (Source D4) for tablets of medicinal product KALETRA, which had been approved after the priority date of the patent of Ukraine for invention No. UA89220, and the invention protected by this patent was the base of it "Cmax and AUC indicators did not show any significant clinical changes after administration of Kaletra tablets with food as compared with fast conditions administration" (the Source **D4**, page. 8, 5th text paragraph from the top), "Kaletra tablets can be used with or without food" (the Source **D4**, page. 28, 5th text paragraph from the top).*

So the characteristic of the independent claim 25 of the formula "the indicated dosage form is administered by a patient with no food or in fasting conditions" is irrelevant, since the achievement of technical result, namely, effective treatment of HIV/AIDS is possible regardless of the method of administration of the solid pharmaceutical dosage form and achievement of technical result is conditioned only by the features (significant characteristics) of solid pharmaceutical dosage form used in method of treatment . According to the Article 6.6.1. of the Rules [3]: "The essence of the invention is a combination of fundamental features sufficient to achieve a technical result which provides the invention (utility model)". In other words, the

characteristics are substantial if they affect the technical result that can be achieved, i.e. are in cause-and-effect relationship with the mentioned result." In the case of the totality of characteristics as for an independent claim 25 of the patent of Ukraine for invention No. UA89220 there is no cause-and-effect relationship between a use of solid pharmaceutical dosage form and technical result, namely, effective treatment of HIV/AIDs. Therefore, the characteristic as to the administration schedule of dosage form is not taken into account because it is irrelevant.

*Sources **D1** and **D2** separately described the way to treat HIV/AIDs, which includes the introduction of solid dosage form to patients who need such treatment, provided that the specified dosed form contains the insoluble form of lopinavir.*

*That is, **the object of the invention under an independent claim 27 of the patent of Ukraine for invention No. UA89220 is a part of prior art of the invention and, therefore, does not meet the "novelty" requirement of patentability.***

*The difference of suggested method of HIV/AIDS treatment in the patent of Ukraine for invention No. UA89220 is the administration of the specified dosing form with no food or in conditions of fast. At the same time Source **D1** and **D2** doesn't provide any instructions as to administration schedule of the well-known solid pharmaceutical dosage form, which should be used after a meal (with food), or under fasting condition. It is confirmed by the description of the patent of Ukraine for invention No. UA89220 (column 36, 4th text paragraph from the top) "Dosed form of this invention shows no effect of food ", i.e., bioavailability of solid pharmaceutical dosage form used for the treatment of HIV/AIDS does not depend on administration schedule of dosage form - after meal (with food), or under fasting condition. This is also confirmed by an approved instruction (Source **D4**) for tablets of medicinal product KALETRA with lopinavir, which had been approved after the priority date of the patent of Ukraine for invention No. UA89220, and the invention protected by this patent was the base of it «Cmax and AUC indicators did not show any significant clinical changes after administration of Kaletra tablets with food as compared with fast conditions administration" (the Source **D4**, page. 8, 5th text paragraph from the top), "Kaletra tablets can be used with or without food" (the Source **D4**, page. 28, 5th text paragraph from the top).*

*So the characteristic of independent claim of Article 27 of the formula "the indicated dosage form is administered by a patient with no food or in fasting conditions" is irrelevant, since the achievement of technical result, namely, effective treatment of HIV/AIDS is possible regardless of the method of administration of the solid pharmaceutical dosage form and achievement of technical result is conditioned only by the features (significant characteristics) of solid pharmaceutical dosage form used in method of treatment. This dosage form is described in dependent claims 28-33 of the patent of Ukraine for invention No.UA89220 that were known and described is Sources **D1** and **D2**. According to the Article 6.6.1. of the Rules [3]: "The essence of the invention is a combination of fundamental features sufficient to achieve a technical result which provides the invention (utility model). In other words, the characteristics are substantial if they affect the technical result that can be achieved, i.e. are in cause-and-effect relationship with the mentioned result." In the case of the totality of*

characteristics as for an independent claim 27 of the patent of Ukraine for invention No. UA89220 there is no cause-and-effect relationship between a use of solid pharmaceutical dosage form and technical result, namely, effective treatment of HIV/AIDs. Therefore, the characteristic as to the administration schedule of dosage form is not taken into account because it is irrelevant.

Given the fact that the objects of the invention under independent claims 1, 25 and 27 do not meet the "novelty" requirement of patentability, pursuant to the provisions of Rules [2] and the Guidelines [6] the examination of the compliance with the conditions of patentability "inventive level" is not performed, because the mentioned objects automatically do not meet the "inventive level" patentability requirement because it is obvious for an expert that it is clearly derived from technology level.

Based on the above mentioned, it is obvious that the objects of the invention, namely the methods of treatment of HIV/AIDs as for independent claims 1, 25 and 27 of the patent of Ukraine for invention No. UA89220 does not meet the conditions of patentability - "novelty" and "inventive level".

Based on the research it is concluded that **the invention under the patent of Ukraine No.UA89220 Ukraine does not meet the requirements of patentability by "novelty" and "inventive level" for the priority date.**

REPORT

The invention under the patent No.UA89220 Ukraine does not meet the requirements of patentability by "novelty" and "inventive level at the priority date.

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