Trilateral Project WM4

Comparative studies in new technologies

(biotechnology, business methods, etc.)

Report on comparative study on protein 3-dimensional (3-D) structure related claims

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European Patent Office
Japan Patent Office
United States Patent and Trademark Office

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Comparative studies in new technologies

Theme: Comparative study on
"protein 3-dimensional (3-D) structure related claims"

1. Introduction

As more 3-D chemical structures are elucidated, such as the 3-D structures of proteins, it is expected that patent applicants will file increasing numbers of applications claiming inventions relating to such 3-D structural information. Given this expectation, the three Offices agreed to conduct a comparative study to enhance mutual understanding concerning the examination of 3-D structure related claims.

2. Provisions

Applicable Sections / Articles of Respective Patent Laws

	Patent Eligible Subject Matter / Statutory Invention	Industrial Applicability / Utility	Enablement / Support / Sufficiency / Written Description and Clarity	Novelty / Inventive step / Nonobviousness
EPO	52	57	83, 84	54,56
JPO	2(1)	29 (1)	36 (4) (6)	29(1)(2)
USPTO	101	101	112	102,103

EPO

EPC Art.52: Patentable Inventions

EPC Art.52(1):

European patents shall be granted for any inventions which are susceptible of industrial application, which are new and which involve an inventive step.

EPC Art.52(2):

The following shall not be regarded as inventions within the meaning of paragraph 1:

(a) discoveries, scientific theories and mathematical methods;

(b) aesthetic creations;

(c) schemes, rules and methods for performing mental acts, playing games or doing business, and programs for computers;

(d) presentations of information.

EPC Art.52(3):

The provisions of paragraph 2 shall exclude patentability of the subject-matter or activities referred to in that provision only to the extent to which a European patent application or European patent relates to such subject-matter or activities as such.

EPC Art.54: Novelty

EPC Art.54(1):

An invention shall be considered to be new if it does not form part of the state of the art.

EPC Art.54(2):

The state of the art shall be held to comprise everything made available to the public by means of a written or oral description, by use, or in any other way, before the date of filing of the European patent application.

EPC Art.56: Inventive Step

An invention shall be considered as involving an inventive step if, having regard to the state of the art, it is not obvious to a person skilled in the art.....

EPC Art.57: Industrial Application

(Art.57) "An invention shall be considered as susceptible of industrial application if it can be made or used in any kind of industry, including agriculture."

(Guidelines C-IV 4.6) In general it is required that the description of a European patent application should, where this is not self-evident, indicate the way in which the invention is capable of exploitation in industry. In relation to sequences and partial sequences of genes this general requirement is given specific form in that the industrial application of a sequence or a partial sequence of a gene must be disclosed in the patent application. A mere nucleic acid sequence without indication of a function is not a patentable invention...

EPC Art.83: Sufficiency of Disclosure

(Art.83) "The European patent application must disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art"

(Guidelines C-II, 4.9) "The application must contain sufficient information to enable the

person skilled in the art, using his common general knowledge, to perform the invention over the whole area claimed without undue burden and without needing inventive skill."

EPC Art.84: Clarity and Support

(Art. 84) "The claims shall define the matter for which protection is sought. They shall be clear and concise and be supported by the description."

(Rule 29(1)) "The claims shall define the matter for which protection is sought in terms of the technical features of the invention"

(Guidelines C-III 6.3) In order to comply with the requirement of Art. 84, there must be sufficient support of technical character in the description that allows to extend the particular teaching of the description to the whole field claimed.

JPO

Japanese Patent Law Sect. 2(1): Definition of Invention

(Guidelines Part II,Chap.1, 1.) Patent Law Section 2(1) defines a statutory invention as a highly advanced creation of technical ideas utilizing a law of nature.

Japanese Patent Law Sect. 29, First Sentence: Industrially Applicable Inventions

(Guidelines Part VII,Chap.2, 1.3.1) "Inventions ... whose utility is not described in a specification or cannot be inferred, do not meet the requirements set forth in the first sentence in Section 29(1) of the Patent Law."

Japanese Patent Law Sect. 29(1): Novelty

(Sect. 29(1)) Any person who has made an invention which is industrially applicable may obtain a patent therefor, except in the case of the following inventions:

(i) inventions which were publicly known in Japan or elsewhere prior to the filing of the patent application;

(ii) inventions which were publicly worked in Japan or elsewhere prior to the filing of the patent application;

(iii) inventions which were described in a distributed publication or made available to the public through electric telecommunication lines in Japan or elsewhere prior to the filing of the patent application.

Japanese Patent Law Sect. 29(2): Inventive Step

(Sect. 29(2)) Where an invention could easily have been made, prior to the filing of the patent application, by a person with ordinary skill in the art to which the invention pertains,

on the basis of an invention or inventions referred to in any of the paragraphs of Subsection (1), a patent shall not be granted for such an invention notwithstanding Subsection (1).

Japanese Patent Law Sect. 36(4) :Description, Enablement

(Guidelines Part VII, Chap. 2, 1.1.2.1) "Section 36(4) of the Patent Law states that "the detailed description of the invention shall be stated....in such a manner sufficiently clear and complete for the invention to be carried out by a person having ordinary skill in the art to which the invention pertains." ...For an invention of a product, the definition of "being able to carry out the invention" is to make and use the product..."

Japanese Patent Law Sect. 36(6): Clarity of Claims

(Guidelines Part VII, Chap. 2, 1.1.1) "According to Section 36(6)(ii) of the Patent Law, the invention for which a patent is sought shall be clear, therefore, scope of claim shall be described so that an invention is clearly identified on the basis of statements of each claim."

USPTO

35 U.S.C. § 101: Patent Eligible Subject Matter

To be considered patent eligible subject matter under 35 U.S.C. § 101, the claimed invention must be a process, machine, manufacture, or composition of matter that has a practical utility.

35 U.S.C. § 101: Utility

To comply with 35 U.S.C. § 101, the claimed invention must have at least one specific, substantial, and credible utility that is either asserted in the specification or is well-established.

35 U.S.C. § 102: Novelty

A claimed invention complies with the novelty requirement if there is no single reference that expressly, implicitly or inherently describes the invention including each claimed element.

35 U.S.C. § 103: Nonobviousness

A claimed invention complies with the nonobviousness requirement if there are no prior art references that, alone or in proper combination, teach or suggest the invention as a whole including each element of the claimed invention. In determining whether an invention would have been obvious, the examiner determines the scope and contents of the prior art,

ascertains the differences between the prior art and the claims in issue, resolves the level of ordinary skill in the art, and evaluates any objective evidence of nonobviousness.

35 U.S.C. § 112, first paragraph: Enablement

To comply with the enablement requirement of 35 U.S.C. § 112, first paragraph, the specification must enable one skilled in the art to make and use the claimed invention without undue experimentation. Factors to be considered in determining whether any required experimentation is "undue" include the breadth of the claims, the nature of the invention, the state of the prior art, the level of ordinary skill in the art, the level of predictability in the art, the amount of direction provided by the inventor, the presence or absence of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

35 U.S.C. § 112, first paragraph: Written Description

To comply with the written description requirement of 35 U.S.C. § 112, first paragraph, the specification must describe the claimed invention in sufficient detail such that one skilled in the art reading the description would recognize that the inventor had invented the claimed subject matter and had possession of the invention as claimed at the time the application was filed. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention.

Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention.

35 U.S.C. § 112, second paragraph: Claim Definiteness

To comply with the claim definiteness requirement of 35 U.S.C. § 112, second paragraph, each claim must particularly point out and distinctly claim the subject matter which the applicant regards as his or her invention. A claim is definite if one skilled in the art would be reasonably apprised of the scope of the claim when the claim is read in light of the specification.

3. Questions Common to All Cases

The answers to the following questions are intended to set forth the perspective of each Office in addressing the patentability of 3-D structure related inventions. Please provide an answer to each question.

1. Are the following claims directed to patent eligible subject matter? If not, explain why and answer questions 2-4 below to the extent possible. If yes, answer questions 2-4 below.

2. Do the following claims satisfy the industrial applicability or utility requirements? If not, explain why.

3. Do the following claims satisfy clarity, enablement, support and written description requirements? If not, explain why.

4. Do the following claims satisfy novelty requirement and the inventive step or nonobviousness requirements? If not, explain why.

5. If there are any comments on the kind of evidence, argument, and/or claim amendment that may overcome any rejection for failure to satisfy the requirements of 1-4 above, please state them.

4. Cases

Case 1: 3-D structural data of a protein per se

[Claim 1]

A computer model of protein P generated with the atomic coordinates listed in Fig. 1.

[Claim 2]

A data array comprising the atomic coordinates of protein P as set forth in Fig. 1 which, when acted upon by a protein modeling algorithm, yields a representation of the 3-D structure of protein P.

[Background]

-The specification asserts that protein P is a novel protein.

-The description gives experimental data and explains that the protein, when active, lowers blood pressure.

-Protein modeling algorithms are well known in the art.

-The description also gives the atomic coordinates of protein P, and asserts these coordinates would be useful in *in silico* (computer-assisted) screening methods.

[Prior Art]

- A search of the prior art did not identify any references that teach or suggest protein P.

Case 2: Computer-readable storage medium encoded with structural data of a protein

[Claim 1]

A computer-readable storage medium encoded with the atomic coordinates of protein P as shown in Fig. 1.

[Background and prior art]

Same as in Case 1.

Case 3: Protein defined by its tertiary structure

[Claim]

An isolated and purified protein having the structure defined by the structural coordinates as shown in Fig. 1.

[Background]

-The description sets forth the 3-D structure of protein P, including the coordinates of the amino acid side chains, the source organism for protein P and the molecular weight of protein P.

-The description gives experimental data and explains that administering protein P lowers blood pressure.

-The structural coordinates were derived from a solution phase protein by NMR at 0.2nm resolution.

[Prior art]

- A search of the prior art did not identify any references that teach or suggest the 3-D structure of protein P.

-The prior art teaches a protein from the same source organism having the same specific function and approximately the same molecular weight.

Case 4: Crystals of known proteins

[Claim]

A crystalline form of protein P having unit cell dimensions of a=4.0nm, b= 7.8nm, and c= 11.0nm.

[Background]

-A nucleotide sequence encoding the amino acid sequence of protein P was known in the art.

-The description explains that administering protein P was previously known to result in lowering blood pressure.

-The inventors assert they have newly produced a stable crystalline form of protein P.

-Protein P in crystalline form is inactive.

-The description gives experimental data with explanations of how to make the crystals.

-Common prior art methods used in protein P crystallization were unsuccessful, and there was clearly a technical difficulty in producing the claimed crystalline form of protein P.

[Prior art]

-There was no prior art reference teaching or suggesting a crystal of protein P or related proteins.

-There was no prior art reference concerning the crystallization method of protein P.

Case 5: Binding pockets and protein domains

[Claim 1]

An isolated and purified molecule comprising a binding pocket of protein P defined by the structural coordinates of amino acid residues 223, 224, 227, 295, 343, 366, 370, 378 and 384 according to Figure 1.

[Claim 2]

An isolated and purified polypeptide consisting of a portion of protein P starting at one of amino acids 214 to 218 and ending at one of amino acids 394 to 401 of protein P as set forth in SEQ ID NO: 1.

[Background]

-Protein P is a previously known protein whose amino acid sequence was also previously known.

-The description explains that administering protein P was previously known to result in lowering blood pressure.

-The inventors assert they have newly discovered that the active residues in the binding pocket of protein P consist of amino acids 223, 224, 227, 295, 343, 366, 370, 378 and 384.

-The description teaches that the possible peptides that begin with any amino acid from position 214 to 218 and end with any amino acid from position 394 to 401 of SEQ ID NO: 1 are protein domains that are able to fold into an active binding pocket of protein P. This ability was confirmed by X-ray diffraction data.

-The description also provides evidence that the above domain alone shows a significantly higher signaling activity compared to the whole protein P when activated by a natural ligand of protein P.

[Prior art]

-Prior art suggesting the position of the binding pocket of protein P was not found.

-Prior art suggesting a protein structure domain containing said binding pocket was also not found.

Case 6: *In silico* screening methods directed to a specific protein (1)

[Claim 1]

A method of identifying compounds that can bind to protein P, comprising the steps of:

applying a 3-dimensional molecular modeling algorithm to the atomic coordinates of protein P shown in Fig. 1 to determine the spatial coordinates of the binding pocket of protein P; and

electronically screening the stored spatial coordinates of a set of candidate compounds against the spatial coordinates of the protein P binding pocket to identify compounds that can bind to protein P.

[Background]

-Protein P is a previously known protein whose amino acid sequence was also previously known.

-The description explains that the activity of protein P was previously known to result in lowering blood pressure.

-The description gives the atomic coordinates of protein P (raw data of the protein itself without any ligands bound to it) but does not describe the position of its binding pocket.

-Instead, the specification gives general information on programs which predict the binding pocket of proteins (which often give a relatively large number of amino acids related to the binding) and general information on commonly used *in silico* screening programs.

-Methods of peptide modeling and binding using rational drug design are well known in the art.

-There was clearly a technical difficulty in obtaining the claimed atomic coordinates of protein P.

-The specification speculates that by using the binding pocket prediction program and in silico screening program, the person skilled in the art can identify compounds binding to said protein.

-The description gives no working examples of identifying compounds using the atomic coordinates of protein P.

[Prior art]

-No prior art suggesting the 3-D coordinates of protein P was found.

-The prior art teaches computer programs that predict the binding pocket of proteins.

-Several *in silico* screening programs using the predicted binding pocket of proteins are also previously known.

Case 7: *In silico* screening methods directed to a specific protein (2)

[Claim 1]

A method of identifying compounds which can bind to protein P by comparing the 3-D structure of candidate compounds with the 3-D molecular model shown in Fig. 5 which comprises the following steps:

(1) ...

(2) ...

(..) ...

(n) ...

(The 3-D molecular model of Fig. 5 presents the positions of heteroatoms in the amino acids constituting the binding pocket of protein P (i.e., amino acids 223, 224, 227, 295, 343, 366, 370, 378 and 384) wherein said heteroatoms can form hydrogen bonds with hydrogen bonding functional groups in a candidate compound.

Steps (1) through (n) describe a data processing method in which

a) the coordinate data of the 3-D molecular model of Fig. 5 is input in a data structure such that the interatomic distances between the atoms of protein P are easily retrieved, and

b) the distances between hydrogen-bonding heteroatoms of different candidate compounds and the heteroatoms that form the binding pocket in the 3D molecular model are compared thereby allowing the identification of those candidate compounds which would theoretically form the most stable complexes with the 3-D molecular model binding pocket of protein P, based on optimal hydrogen bonding between the two structures.)

[Claim 2]

A compound identified by the method of claim 1.

[Claim 3]

A database encoded with data comprising names and structures of compounds identified by the method of claim 1.

[Background]

-Protein P is a previously known protein whose amino acid sequence was also previously known.

-The description explains that the activity of protein P was previously known to result in lowering blood pressure.

-The description gives the atomic coordinates of protein P as a co-crystal with its natural ligand, and gives a logical explanation that the active residues in the binding pocket of

protein P consists of amino acids 223, 224, 227, 295, 343, 366, 370, 378 and 384.

-The description explains how the 3-D molecular model of Fig. 5 includes the 3-D structure of the binding pocket of protein P.

-The description gives working examples of the claimed method in which a number of compounds are identified.

-The description also shows experimental data of the actual binding affinities of the compounds identified. According to the data shown, the person skilled in the art can understand that the claimed method can actually identify a number of compounds which bind strongly enough to protein P so that some biological effect can be expected.

[Prior art]

-No prior art suggesting the 3-D coordinates of protein P was found.

-The prior art teaches *in silico* screening programs that compare the 3-D structure of candidate compounds with the 3-D molecular model of the binding pocket of a protein of interest.

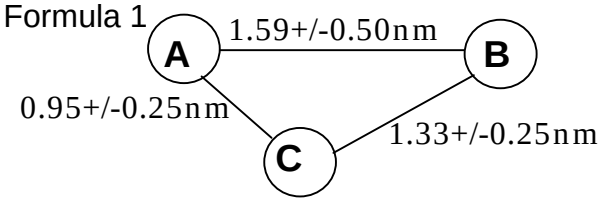
-The method of storing coordinate data to optimize the interatomic distance information is taught by the prior art.

Case 8: Pharmacophores and pharmacophore - defined compounds (pharmacophores defined by the distance between atom-groups)

[Claim 1]

A pharmacophore having a spatial arrangement of atoms within a molecule defined by the following formula:

Formula 1



in which A and B both represent an electron donor atom, C represents a carbon atom that is part of a hydrophobic group, and the distances represent the distances between the centers of the respective atoms.

[Claim 2]

An isolated compound or its salt defined by the pharmacophore in claim 1.

[Background]

- A pharmacophore is a description of a generalized concept of molecular features in terms of information on spatial arrangement of chemical elements (e.g. hydrophobic groups, charged/ionizable groups, hydrogen bond donors/acceptors, and substructures) that are considered to be responsible for a desired biological activity.

-Protein P is a previously known protein whose amino acid sequence was also previously known.

-The description explains that the activity of protein P was previously known to result in lowering blood pressure.

-A search of the prior art did not identify any references that teach or suggest the 3-D structure of protein P.

-The description teaches that the pharmacophore shown in formula 1 was evaluated from the 3-D structure of the ligand binding pocket of protein P.

-The description also teaches that the structure of the ligand binding pocket of protein P was estimated using conventional methods.

-The description also describes that a novel ligand was designed based on the pharmacophore, and shows experimental results that the ligand binds to the protein with relatively high affinity.

[Prior Art]

-A document showing an agonist of protein P was found.

5. Summary of the Cases

		Case
Data	Computer model of protein	Case 1 (Claim 1)
	Data array comprising atomic coordinates of protein	Case 1 (Claim 2)
	Computer-readable storage medium encoded with atomic coordinates of protein	Case 2
	Database encoded with data comprising names and structures of compounds	Case 7 (Claim 3)
	Pharmacophore	Case 8 (Claim 1)

		Exact polypeptide is known.	Case
Protein	Protein having the structure defined by structural coordinates	*Prima facie* identical	Case 3
	Crystalline form of protein	Not crystalline form-Yes/ Crystalline form-No	Case 4
	Polypeptide comprising a binding pocket of protein defined by a structural coordinates	No(partially Yes)	Case 5 (Claim 1)
	protein domains that begin and end with specific residue	No	Case 5 (Claim 2)

	Steps involved in the process	Position of protein binding pocket	Working examples of identifying compounds.	Case
in silico screening method	described	not described	none	Case 6
	described	described	described	Case 7 (Claim 1)

		Working examples of identifying compounds.	Case
Compound	Identified by an *in silico* screening method	described	Case 7 (Claim 2)
	Defined by a pharmacophore	described	Case 8 (Claim 2)

6. Answers

A) Data (Case 1, Case 2, Claim 3 of Case 7, Claim 1 of Case 8)

Patent Eligible Subject Matter / Statutory Invention

The three Offices concluded that claims in Case 1, Case 2, Claim 3 of Case 7 and Claim1 of Case 8 are not patent eligible subject matter or statutory inventions. The claimed computer model, data array and computer-readable storage medium encoded with the atomic coordinates, database encoded with data comprising names and structure, and the pharmacophore are mere presentations of information or abstract ideas which have not been practically applied.

Other Comments

(EPO) Case 1: It is non-technical by not solving a technical problem, and it does not have a technical effect in itself. A search of this claim will not be carried out according to Rule 45 EPC.

Case 2: It is noted that in a particular circumstance a "Technical Board of Appeal" has decided (**T1173/97**, OJ 1999, 609) that the information encoded on a computer-readable storage medium can be patentable, ie can be regarded as an invention which is susceptible of industrial application and which is new and which involves an inventive step. The data encoded on the medium concerned a computer program considered in this special case to have a technical character by having a further technical effect (EPO Guidelines Part C Chapter IV.2).

Claim 3 of Case 7: A search of this claim will not be carried out according to Rule 45 EPC.

Claim 1 of Case 8: The use of the distances between the atoms as parameters in the present context is considered to lead to a lack of clarity within the meaning of Article 84 EPC. It is impossible to compare these parameters with what is set out in the prior art. The lack of clarity is such as to render a meaningful complete search impossible.

(JPO) Case 1: It is neither directed to a presentation of information with some technical feature in the presentation or the means or method of presentation, nor is it directed to a data structure which concretely realizes information processing using hardware resources. There may be cases where data is a statutory invention if it is featured by data structure (logical structure of data defined by interrelationship among data elements) and information processing by the data structure is concretely realized by using hardware resources.

Case 2: Presentation of information (where the technical feature is found only within the contents of the information, and the main purpose of the invention is to present such information) without any technical feature in the presentation or the means or method of presentation, is not an “invention”.

Claim 3 of Case 7: The claim is neither directed to a presentation of information with a technical feature in the presentation or the means or method of presentation, nor is it directed to a data structure which concretely realizes information processing using hardware resources.

Claim 1 of Case 8: The only technical features of a pharmacophore are found within the contents of the information.

(USPTO) Case 1: Claim 1, directed to a computer model, is not tangibly embodied and therefore is nonfunctional descriptive material *per se*. Descriptive material is considered to be an abstract idea and therefore the claim would be rejected under 35 U.S.C. § 101 as not claiming patent eligible subject matter. Claim 2, directed to a data array, claims a compilation or mere arrangement of data. The 3-D coordinates of a protein constitute nonfunctional descriptive material without physical structure, and therefore are abstract ideas that are not patent eligible subject matter under 35 U.S.C. § 101. See, e.g., *In re Warmerdam*, 33 F.3d 1354, 1361, 31 USPQ2d 1754, 1760 (Fed. Cir. 1994) (descriptive material per se is not patent eligible subject matter).

Case 2: As claimed, the protein data stored on the computer-readable medium is merely stored so as to be read by a computer without creating any functional interrelationship, either as part of the stored data or as part of the computing processes performed by the computer. Thus the 3-D coordinates do not impart functionality to either the data or the computer, and are therefore nonfunctional descriptive material. Nonfunctional descriptive material stored in a computer-readable medium is an abstract idea that is not patent eligible subject matter under 35 U.S.C. § 101.

Claim 3 of Case 7: The claim is nonstatutory under 35 U.S.C. § 101 because it is an abstract idea not tangibly embodied and is a mere collection of data. *See, e.g., In re Warmerdam*, 33 F.3d 1354, 1361, 31 USPQ2d 1754, 1760 (Fed. Cir. 1994) (descriptive material *per se* is not patent eligible subject matter).

Claim 1 of Case 8: The pharmacophore is merely a generalized concept and not a compound or article of manufacture. As such the pharmacophore is an abstract idea and is not patent eligible subject matter under 35 U.S.C. § 101.

B) Polypeptide (Case 3, Case 4, Claim 1 of Case 5, Claim 2 of Case 5)

Patent Eligible Subject Matter / Statutory Invention

The three Offices concluded that claims in Case 3, Case 4, Claim 1 of Case 5 and Claim2 of Case 5 are patent eligible subject matter or statutory invention as a polypeptide.

Industrial Applicability (Application) / Utility

The three Offices concluded that there was industrial applicability (application)/utility for claims in Case 3, Case 4, Claim 1 of Case 5 and Claim2 of Case 5, since the description explains that administering the protein lowers blood pressure, so the claimed polypeptide complies with the requirement.

Enablement / Support / Clarity and/or Written Description

The three Offices concluded that for Case 3, Case 4 and Claim2 of Case 5, the claim meets the requirement of enablement, support, clarity, and/or written description.

In case 3 the specification discloses the 3-D structure of protein P including the coordinates of the amino acid side chains, the source organism for protein P and the molecular weight of protein P. Based on this information, a person of ordinary skill in the art would be able to make the claimed protein.

In case 4 the claim complies with the above mentioned requirement because the specification teaches how to make the claimed crystals, and one skilled in the art could use the claimed invention without undue experimentation.

In claim 2 of case 5, the claim complies with the above mentioned requirement because it is limited to fragments of protein P that contain the binding pocket and were shown in the specification to retain binding activity and the signaling activity of protein P.

The three Offices concluded that for Claim 1 of Case 5, the claim does not meet the requirement of enablement, support, clarity, and/or written description.

The claim recites a “molecule” defined only by the “structural coordinates” of 9 amino acid residues from a source polypeptide of at least 161 residues. The claim only defines a portion of the claimed molecule; those portions of the claimed molecules other than “a binding pocket” are undefined. Therefore, the claim does not meet clarity.

Novelty and/or Inventive Step

The three Offices concluded that for Case 3 and Claim 1 of Case 5, the claim lacks novelty.

In case 3 since the prior art teaches a protein from the same source organism having the same specific function and approximately the same molecular weight, there is a reason to

expect that the claimed protein would be prima facie identical with the protein of the prior art.

In case 5, Claim 1 recites open “comprising” language, and thus the claim encompasses natural protein P, which is known in the prior art.

Other Comments

(EPO) Case 3: If the applicant provides evidence for the novelty over the prior art protein, novelty and inventive step can be accepted (it is noted that it is presently considered that the structural data at high resolution fully define the protein, including the deducible primary sequence).

Case 4: It may be advantageous to produce the protein in eg a stable form (and high purity) and also to use the crystals for determination of the 3-D structure, the atomic coordinates useful in *in silico* screening methods and rational drug design.

Claim 1 of Case 5: The wording "molecule" is considered as undesirable, as a single molecule is not enabled.

Claim 2 of Case 5: It is assumed that the description gives sufficient detail to accept that the variable ends of the polypeptide portion are not relevant to the blood pressure lowering activity of the claimed portion.

(JPO) Case 3: If the applicant is able to submit enough evidence that the claimed protein is different than the protein described in prior art, the reason for refusal will be cleared. Furthermore, if the claimed protein, having the same amino acid sequence as a known protein, has a different 3-D structure compared to the known protein (e.g., abnormal prion protein compared to and normal prion protein), the former is considered novel.

In such a case, however, we believe the applicant would rather define the protein by its amino acid sequence and physical properties other than its structural coordinates.

Case 4: Even if protein P that is able to lower blood pressure in active form is inactive in crystalline form, it is considered that the protein is able to be restored to the active form by well known art. So the claim is clear and fulfils enablement. The protein crystal is considered novel, since it differs its form and structure from the protein itself (a compound). Since the prior art does not teach any crystalline forms of protein P or any methods to obtain the claimed crystalline protein P, and since common methods used in protein crystallization were unsuccessful, the crystal involves inventive step.

Claim 1 of Case 5: Except for binding pockets, concrete conformation of the mo-

lecule is unclear. Therefore, the claim does not meet clarity requirements.

"A binding pocket" will not fold into its proper 3-D structure unless you have the whole protein or a whole structural domain (meaning that you have to "cut" the amino acid sequence at the right place in order to have a structural domain that folds into the correct 3-D structure). Protein P in crystalline form can be made with the description.

It is not possible to make the real compound defined by the structural coordinates of said amino acid residues with referring to the description.

Therefore, the claim contains a part that does not meet enablement requirement.

Claim 2 of Case 5: Polypeptides are protein domains that can fold into an active binding pocket of protein P. By expressing the said polypeptide, a person skilled in the art can get easily protein which has active binding pocket.

Therefore, the claim meets enablement.

We can understand the difference between the claimed polypeptide and the whole protein P. Thus the claimed invention is considered novel.

Prior art does not teach any polypeptide which consists of a specific part of protein P, or methods to specify parts of the polypeptide, and the claimed polypeptide shows a significantly higher signaling activity compared to the whole protein P.

Therefore, the claimed polypeptide meets involves inventive step requirement.

(USPTO) Case 3:

Under USPTO practice, when an applicant claims a composition in terms of a property or characteristic, and the composition of the prior art appears to be the same as that of the claimed composition but the property or characteristic is not explicitly disclosed by the reference, the examiner rejects the claims as anticipated by, or, in the alternative, as obvious over the reference, supporting the rejection with evidence or reasoning supporting the inherency of the disclosed property. This shifts the burden to applicant to show a nonobvious difference over the reference. See, e.g., In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985); In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977).

Those principles would be applied to this case. The initial search would generally be limited to a conventional prior art search. The examiner would do a text search with initial search terms directed to the genus and/or species of organism from which the claimed protein was prepared along with an approximate molecular weight. (Note: Searching on the basis of molecular weight is difficult because molecular weight estimations vary depending on the technique employed.) Evi-

dence of effects on blood pressure associated with any protein found from this search would also be considered. If the 3D structure is sufficient to derive amino acid sequence information, a search against appropriate protein and nucleic acid databases would also be performed.

In this case, the prior art teaches a protein from the same source organism having the same specific function and approximately the same molecular weight. Although the prior art does not teach the atomic coordinates as claimed, the atomic coordinates are an inherent property or characteristic of the claimed protein in a particular state. Absent evidence that the state defined by the coordinates represents a form distinguishable from that for the protein present in the prior art, the claim would be rejected under 35 U.S.C. § 102 as being anticipated by, or in the alternative, under 35 U.S.C. § 103 as obvious over, the prior art protein. This situation is analogous to the situation where a claimed protein is characterized by amino acid sequence, but is otherwise identical to a prior art protein that has not yet been sequenced.

Applicant may overcome the rejection by submitting evidence showing that the prior art protein is not the same as, or an obvious variant of, the protein described in the prior art. With respect to the written description requirement, applicant has provided sufficient structural information so that one skilled in the art would recognize that applicant was in possession of the invention as claimed.

Case 4: With respect to the how-to-use prong of the enablement requirement, assuming that the claims comply with the utility requirement of 35 U.S.C. § 101, it is necessary to determine whether one skilled in the art could use the claimed invention without undue experimentation. With respect to novelty, it is recognized in the art that a crystal of protein P is different from previously known forms of protein P. Furthermore, the claim complies with the nonobviousness requirement of 35 U.S.C. § 103 because as noted in the fact pattern, there was no prior art reference teaching or suggesting a crystal of protein P or related proteins. Although there is a general desire to obtain the crystal structure of any protein, the methodology of doing so is unpredictable and specific to each individual protein. Therefore, without guidance in the art as to how to crystallize a particular known protein, the known protein in crystalline form would be nonobvious.

Claim 1 of Case 5: Claim 1 would be rejected under 35 U.S.C. § 112, first para-

graph as lacking written description and as encompassing a broader scope than is enabled by the specification. The claim lacks written description because it recites a "molecule" defined only by the "structural coordinates" of 9 amino acid residues from a source polypeptide of at least 161 residues. The recited structure is open-ended and defines only a portion of the claimed molecule. The molecule may be a polypeptide but it may also include residues that are not amino acids or amino acid derivatives. Protein P and the 40 fragments shown to be active all have the naturally occurring amino acid sequence of protein P and do not constitute a representative number of species of the claimed genus, which includes polypeptide and non-polypeptide molecules, to allow one of skill in the art to envision all members of the genus. Thus they do not provide an adequate written description for the genus.

With respect to the enablement requirement, the specification enables the full-length protein P and the specifically disclosed fragments, but the specification does not enable all molecules encompassed by claim 1. For the binding pocket to function, the 9 residues must be in the same spatial relationship to each other as they are in the natural polypeptide or the polypeptide fragments disclosed in the specification. Because of the large number of residues within the pocket that can be changed to comprise any one of 20 amino acids (or possibly other unspecified structural elements), and the fact that additional unspecified moieties may be included on either end of the binding pocket, the total number of molecules that are encompassed by this claim is extremely large. Because of the vast number of species encompassed by the claimed genus and the lack of guidance as to what structural changes may be made in the amino acid sequence between and around the active residues such that the resulting polypeptide would retain the 3-dimensional structure and activity of the binding pocket, it would require undue experimentation to make and use the invention over the entire scope claimed in claim 1.

Claim 2 of Case 5: Claim 2 is limited to fragments of protein P that consist of the amino acid residues that make up the binding pocket and retain binding and signaling activity. These fragments were not disclosed in the prior art and would not have been obvious on the basis of the known amino acid sequence of the entire protein P.

C) *In silico* screening method (Case 6, Claim 1 of Case 7)

Patent Eligible Subject Matter / Statutory Invention

The three offices concluded that claim 1 of case 7 contains patent eligible subject matter or refers to a statutory invention.

Industrial Applicability (Application) / Utility

The three Offices concluded that case 6 and claim 1 of case 7 in both cases may fulfil the requirements of industrial applicability/utility.

Enablement / Support / Clarity and/or Written Description

The three offices concluded that claim 1 of case 7 may fulfil the requirements of sufficiency/enablement, clarity, support, and written description.

Novelty and/or Inventive Step

A common opinion of the offices about the involvement of an inventive step cannot be presented.

Other Comments

(EPO) Case 6:

An in silico screening method is considered to be a patentable invention under Article 52(2) and 52(3) of the EPC; it refers to a method having a link to a technical contribution by the use of technical data. With respect to the sufficiency of disclosure it is noted that, although the applicant may file as support further technical information with examples providing evidence for the correctness of the prediction of the position of the pocket, the method as claimed (in the absence of eg further information on the candidate compounds) is not fully enabled in the absence of any working examples.

Claim 1 of Case 7: An in silico screening method with this wording is considered to be a patentable invention (it is assumed that the 3-D molecular model shown in Fig.5 presents the complete structure of protein P). It refers to a method having a link to a technical contribution characterized by technical feature(s). This activity is not regarded as a presentation of information or as a pure mathematical method, excluded by Article 52(2)(d) or (a) of the EPC, respectively, but to the use of the structural data.

Thus, the subject-matter is directed to patent eligible subject-matter. In addition, the claimed subject-matter may satisfy the requirements clarity, enablement and support (the description gives experimental data including identified compounds). The prior art did not disclose or suggest the 3-D coordinates of protein P. The

claimed method applying the use of the coordinates is therefore considered to be new, non-obvious and industrial applicable.

(JPO) Case 6:

To be qualified as "a creation of technical ideas utilizing a law of nature," a claimed invention must be concrete enough to accomplish a certain purpose.

If the claimed invention is considered to be computer software-related inventions where information processing by software is not concretely realized by using hardware resources, the claimed invention does not constitutes "a creation of technical ideas utilizing a law of nature."

Therefore, the claim is not a statutory invention.

If the claimed invention is considered a software-related invention it only differs from the prior art by the limitation based on Figure 1 coordinate data.

Claim 1 of Case 7: To be qualified as "a creation of technical ideas utilizing a law of nature," a claimed invention must be concrete enough to accomplish a certain purpose.

If the claimed invention is considered to be a computer software-related invention and where information processing by software using hardware resources is concretely described, the claim is a statutory invention.

Claimed invention is a method of identifying compounds that bind to protein P and may normalize blood pressure.

Therefore, the claim meets industrial applicability requirements.

The description gives evidence that compounds identified by using the atomic coordinates bind strongly enough to protein P so that some biological effect can be expected

Therefore, the claim meets enablement requirements.

The claimed invention is considered a computer software-related invention with the technical feature of an information processing method by software.

The difference between the prior art and the claimed invention as a whole is limited to the 3-D molecular model shown in Fig. 5.

Data that does not alter the processing method should be considered as mere contents. Technical specifications cannot be affirmatively inferred even if the limitation of a 3-D molecular model is added to the claim.

(USPTO) Case 6:

To qualify as patent eligible subject matter, the invention of claim 1, as a whole, must accomplish a practical application. That is, it must produce a "useful, concrete and tangible result." State Street Bank & Trust Co. v. Signature Financial Group Inc., 149 F.3d 1368, 1373, 47 USPQ2d 1596, 1601-02 (Fed. Cir. 1998). Note that the "useful result" aspect of the practical application test requires significant functionality to be present. See Arrhythmia Research Tech. v. Corazonix Corp., 958 F.2d 1053, 1057, 22 USPQ2d 1033, 1036 (Fed. Cir. 1992). This is an inquiry distinct from the test for "utility" as discussed below. Here, the method steps are applicable to a set of structural parameters and the result set provides a number of lead compounds with an increased probability of binding to the protein whose structure was input. Thus, the method provides a useful, concrete and tangible result that can be used to guide further screening. Irrespective of the recitation of specific structural coordinates, the claims are directed to in silico screening methods that have a practical application, and therefore the methods are statutory subject matter under the State Street rationale.

The utility of the claimed method depends on the utility of the candidate compounds identified as a result of the screening methods. The specification teaches that protein P, when active, lowers blood pressure, however there is no indication whether there is a correlation between binding activity and activation. The claims complies with the utility requirement of 35 U.S.C. § 101 if the specification teaches that the binding compounds may be used to either stimulate activity of protein P to reduce blood pressure, or in cases of hypotension, inhibit the activity of protein P to cause an increase in blood pressure. An assertion of either or both of these uses for a protein P binding compound that is credible to one skilled in the art would be accepted as a specific, substantial, and credible utility. However, in the absence of a known or disclosed correlation between binding and activation, identifying compounds which can bind to protein P is not a specific, substantial, and credible utility.

Enablement in this case depends first on choosing, with only general guidance from the specification, one or more programs to identify the binding pocket of protein P, then on demonstrating that the identification of the binding pocket is correct, and finally on the expectation of success in identifying compounds that bind to protein P and the amount and nature of experimentation required to determine which of the candidate compounds would be useful. Unless the binding

pocket identification programs were known to be highly predictive, it is likely that the amount of experimentation required to identify and confirm the binding pocket would be considered undue because the programs would yield multiple possible binding pockets and the skilled artisan would have to choose the most likely predicted binding pocket(s) to test in order to determine the actual pocket. If the binding pocket is not confirmed prior to screening for potential binding compounds, the sets of possible binding compounds could be completely devoid of compounds that bind protein P. Furthermore, even if the claimed methods identified compounds that bind to protein P, the specification does not appear to teach how to use such compounds without undue experimentation.

The claimed method of identifying compounds that bind to protein P comply with the written description requirement of 35 U.S.C. 112, first paragraph. The specification describes prior art programs that can be used to identify the binding pocket and to screen for candidate binding compounds. The specification also describes the structural coordinates of protein P, which are required by the pocket prediction and screening programs. Therefore, the specification describes the elements that are necessary to carry out the claimed method such that one skilled in the art would have recognized that applicant was in possession of the claimed invention.

The claims are novel because the 3-D coordinates are not found in the prior art. The key factor in analyzing the obviousness of these claims over the prior art is the determination that the computer algorithm used to identify compounds that can potentially bind protein P is a known algorithm and is unmodified. If the difference between the prior art and the claimed invention as a whole is limited to descriptive material stored on or employed by a machine, it is necessary to determine whether the descriptive material is functional descriptive material or nonfunctional descriptive material. Data, which are fed into a known algorithm whose purpose is to compare or modify those data using a series of processing steps, do not impose a change in the processing steps and are thus nonfunctional descriptive material. A method of using a known comparator for its known purpose to compare data sets does not become nonobvious merely because new data becomes available for analysis. Nonfunctional descriptive material cannot render nonobvious an invention that would have otherwise been obvious. See *In re Gulack*, 703 F.2d 1381, 1385 (Fed. Cir. 1983) (when descriptive material is not functionally related to the substrate, the descriptive material will not distinguish the in-

vention from the prior art in terms of patentability); *Ex parte Carver*, 227 USPQ 465, 470 (Bd. Pat. App. & Int. 1985)(Messenheimer and Nusbaum, Examiners-in-Chief, concurring)(Recorded signals are accorded patentable weight in determining obviousness where signals are used to actuate and control sound recording responsive device structure to produce appellant's disclosed acoustic phenomena because the signals define a functional relationship of the type referred to in *Gulack*.).

Claim 1 of Case 7: The specification adequately describes and enables one skilled in the art to make the claimed method of screening by virtue of working examples that identified compounds that bind to protein P. The working examples provide sufficient guidance regarding the screening program, and demonstrate the effectiveness of the screening program in using the disclosed 3-D coordinates of protein P to identify ligands that bind with sufficient affinity that a biological effect would be expected by one skilled in the art. With respect to the how-to-use prong of the enablement requirement, the specification teaches that protein P, when active, lowers blood pressure, however there is no indication whether there is a correlation between binding activity and modulation of blood pressure. If compounds that bound protein P could be used to modulate blood pressure without undue experimentation, the claimed method would comply with the enablement requirement of 35 U.S.C. § 112.

Claim 1 is novel because the 3-D molecular model of Fig. 5 is not found in the prior art. The key factor in analyzing the obviousness of these claims over the prior art is the determination of whether the claimed data processing method used to identify compounds that can potentially bind protein P, i.e., steps (1) through (n), would have been obvious to one skilled in the art. See the analysis of Case 6, above. In this case, the fact pattern suggests that the claimed method would have been prima facie obvious over the prior art because steps (1) through (n) appear in the prior art methods.

D) Compound (Claim 2 of Case 7, Claim 2 of Case 8)

Patent Eligible Subject Matter / Statutory Invention

The three Offices concluded that Claim 2 of Case 7 and Claim 2 of Case 8 are patent eligible subject matter or statutory invention as a compound.

Industrial Applicability (Application) / Utility

The three Offices concluded that there was industrial applicability (application)/utility for Claim 2 of Case 7 and Claim 2 of Case 8, since the specification teaches that protein P, when active, lowers blood pressure (provided there is a known or disclosed correlation between binding and activation).

Enablement / Support / Clarity and/or Written Description

The three Offices concluded that for Claim 2 of Case 7 and Claim 2 of Case 8, the claim does not meet the requirement of enablement, support, clarity, and/or written description, since it would require a trial and error effort beyond what is expected of a person having ordinary skill in the art to envisage a ligand structure other than the one described concretely in the examples, and make such compounds.

Other Comments

(EPO) Claim 2 of Case 7: It would appear that a lack of sufficiency of disclosure and/or lack of support should be raised, as the claimed compound has not been enabled over all the whole range of claimed embodiments. (Reach-through claim; see answer for claim 2 of case 8; reference can also be made to the earlier trilateral project B3b report with theme: comparative study on "reach-through claims")

An incomplete search will be carried out for this reach-through claim, limited to the example of the description.

With respect to novelty, it would be the starting position in examination that the natural ligand already in the state of the art is prejudicial to novelty.

Claim 2 of Case 8: The application is not sufficiently enabled, taking into account the scope of the claim embracing an excessively large number of compounds and the fact that the description refers to one novel ligand designed on the basis of the pharmacophore. A lack of support should also be raised according to Article 84 EPC in the light of the EPO Guidelines C-III, 6.3: In order to comply with the requirements of Art.84, there must be sufficient support of technical character in the description that allows to extend the particular teaching of the description to the whole field claimed. In the case of the pharmacophore it is unclear how far the scope extends: the features of the compound concerning the spatial arrangement of the 3 atoms do not support sufficiently the characterization of the compound (a meaningful comparison with the prior art cannot be made (Guidelines C-III, 4.7a).

It is furthermore noted that the natural agonist of protein P will fulfill the structural requirements of the pharmacophore, and therefore would be prejudicial to novelty (and in fact should result also in an objection for lack of unity of invention).

An incomplete search will be carried out for this reach-through claim, limited to the example of the description.

(JPO) Claim 2 of Case 7: When a person skilled in the art cannot conceive a concrete product with such function or characteristics, etc., even by taking into consideration the common general knowledge as of the filing, since the concrete matters pertaining to the invention cannot be understood, the scope of the invention usually cannot be deemed clear.

Claim 2 of Case 8: Claim 2 lacks clarity since it is not clear to a person having ordinary skill in the art what sort of compound would fall under the claim. Novelty and inventive step may be destroyed since the agonist found in the prior art search binds to the ligand binding pocket of protein P, and thus, there is a high probability that this agonist falls into the pharmacophore definition.

In Claim 2 of Case 8, Novelty and inventive step may be destroyed since the agonist found in the prior art search binds to the ligand binding pocket of protein P. Thus there is a high probability that this agonist falls under the pharmacophore definition.

(USPTO) Claim 2 of Case 7: The claimed invention is drawn to a compound identified by the method of claim 2. However, no structural or specific functional characteristics of such a compound is provided. Because one skilled in the art would conclude that the inventors were not in possession of the claimed invention, the claim fails to comply with the written description requirement.

This claim also fails to meet the enablement requirement for the "how to make" prong of 35 U.S.C. § 112, first paragraph. The fact pattern fails to disclose any particular structure for the claimed compound. The specification does not provide any guidance or any working examples in this unpredictable art, and thus the artisan would have been unable to make the claimed compound without undue experimentation. An assertion of either or both of these uses for a protein P binding compound that is credible to one skilled in the art would be accepted as a specific, substantial, and credible utility.

Claim 2 of Case 8: This claim fails to comply with the enablement requirement. With respect to the how-to-make prong of the enablement requirement, the specification only enables the compound that was actually made and tested, since there is no evidence that the specification provides sufficient guidance regarding how to choose an array of specific atom groups that could form compounds that would fit the general formula, and how to test the compounds such that making and testing would not constitute undue experimentation. With re-

spect to the how-to-use prong of the enablement requirement, even if the claimed compound meets the utility requirement of 35 U.S.C. § 101, the specification does not teach how to administer the claimed compound so as to effect a viable blood pressure treatment regimen. In the absence of additional information the skilled artisan would not have been able to use the claimed compound(s) for treatment without undue experimentation.

This claim does not comply with the written description requirement of 35 U.S.C. § 112, first paragraph. A large number of possible compounds may fit the pharmacophore formula. However the specification does not set forth a representative number of structures that would allow the person of ordinary skill in the art to conclude that the inventor had possession of the broad scope of the genus invention at the time the application was filed.

7. Summary of Answers

(In the following answers, Y stands for 'Yes', N stands for 'No', N/A stands for ‘not addressed’, and M stands for ‘Maybe’)

EPO

Case	Claim	Patent Eligible Subject Matter	Industrial Applicability	Clarity/ Support	Sufficiency	Novelty and Inventive Step
1	1	**N**	**N/A**	**N/A**	**N/A**	**N/A**
	2	**N**	**N/A**	**N/A**	**N/A**	**N/A**
2	1	**N**	**N/A**	**N/A**	**N/A**	**N/A**
3	1	**Y**	**Y**	**Y**	**Y**	**N**
4	1	**Y**	**Y**	**Y**	**Y**	**Y**
5	1	**Y**	**Y**	**N**	**N**	**N**
	2	**Y**	**Y**	**Y**	**Y**	**Y**
6	1	**Y**	**Y**	**Y**	**N**	**Y**
7	1	**Y**	**Y**	**Y**	**Y**	**Y**
	2	**Y**	**Y**	**N**	**N**	**M**
	3	**N**	**N/A**	**N/A**	**N/A**	**N/A**
8	1	**N**	**N/A**	**N/A**	**N/A**	**N/A**
	2	**Y**	**Y**	**N**	**N**	**N**

JPO

Case	Claim	Statutory Invention	Industrial Applicability	Clarity	Enablement	Novelty and Inventive Step
1	1	**N**	**N/A**	**N/A**	**N/A**	**N/A**
	2	**N**	**N/A**	**N/A**	**N/A**	**N/A**
2	1	**N**	**N/A**	**N/A**	**N/A**	**N/A**
3	1	**Y**	**Y**	**Y**	**Y**	**N**
4	1	**Y**	**Y**	**Y**	**Y**	**Y**
5	1	**Y**	**Y**	**N**	**N**	**N**
	2	**Y**	**Y**	**Y**	**Y**	**Y**
6	1	**N**	**Y**	**N/A**	**N/A**	**N/A(N)**
7	1	**Y**	**Y**	**Y**	**Y**	**N**
	2	**Y**	**Y**	**N**	**N**	**N/A**
	3	**N**	**N/A**	**N**	**N**	**N/A**
8	1	**N**	**N**	**N**	**N/A**	**N/A**
	2	**Y**	**Y**	**N**	**N**	**N**

* To the general scope of the claim

USPTO

Case	Claim	Patent Eligible Subject Matter	Utility	Written Description	Enablement	Novelty and Inventive Step
1	1	**N**	**M**	**Y**	**N**	**N/A**
	2	**N**	**M**	**Y**	**N**	**N/A**
2	1	**N**	**M**	**Y**	**N**	**N**
3	1	**Y**	**Y**	**Y**	**Y**	**N**
4	1	**Y**	**Y**	**Y**	**M**	**M**
5	1	**Y**	**Y**	**N**	**N**	**N**
	2	**Y**	**Y**	**Y**	**Y**	**Y**
6	1	**Y**	**M**	**Y**	**N**	**N**
7	1	**Y**	**M**	**Y**	**M**	**N**
	2	**Y**	**M**	**N**	**N**	**M**
	3	**N**	**N/A**	**N/A**	**N/A**	**N/A**
8	1	**N**	**N/A**	**N/A**	**N/A**	**N/A**
	2	**Y**	**M**	**N**	**N**	**M**

8. Conclusion

Summary of Comments: Fulfillment of Requirements of Patent Eligible Subject Matter, Statutory Invention, Industrial Applicability, Utility, Enablement, Support, Clarity, Written Description, Novelty, Inventive step and/or Nonobviousness

(For the following chart, 'Y' means all the above requirements are met, whereas 'N' means at least one of the requirements are not met, considering the general scope of the claims. 'M' means 'Maybe'.)

Case	Claim	EPO	JPO	USPTO
1	1	N	N	N
	2	N	N	N
2	1	N	N	N
3	1	N	N	N
4	1	Y	Y	M
5	1	N	N	N
	2	Y	Y	Y
6	1	N	N	N
7	1	Y	N	N
	2	N	N	N
	3	N	N	N
8	1	N	N	N
	2	N	N	N

The three Offices shared the following views:

1. The claims for:
   (1) computer models of protein
   (2) data array comprising atomic coordinates of protein
   (3) computer-readable storage medium encoded with atomic coordinates of protein
   (4) database encoded with data comprising names and structures of compounds
   (5) pharmacophore
   are not patent eligible subject matter or statutory inventions.

2. In cases where no references teach or suggest the 3-D structure of protein but there is enough reason to expect that the claimed protein would be prima facie identical with the protein of the prior art, the claim for:
   (1) protein having the structure defined by the structural coordinates

does not comply with the requirements of novelty.

3. A crystalline form of a protein
meets all the requirements of patent eligible subject matter, statutory invention, industrial applicability (application), utility, enablement, support, clarity, written description, novelty, inventive step and nonobviousness
   (a) since a protein is composition of matter of patentable subject or statutory invention, if:
   (b) it is well established in the art that the crystalline form of the protein has utility or industrial applicability, and
   (c) the specification teaches how to make the claimed crystals, and
   (d) one skilled in the art could use the claimed protein crystal without undue experimentation, and
   (e) characterization of the crystal structure is provided in the claim, (e.g., by specifying the cell unit dimensions) and
   (f) there was no prior art reference teaching or suggesting a crystal of the protein or related proteins, and
   (g) there was no particular guidance in the art as to how to crystallize the protein.

4. In cases where a protein is previously known, the claim for:
   (1) An isolated and purified molecule comprising a binding pocket of protein defined by the structural coordinates
   does not comply with all of the requirements of enablement, support, clarity, written description, novelty, inventive step and nonobviousness.

5. An isolated and purified polypeptide consisting of a portion of a protein
with signaling activity meets all the requirements of patent eligible subject matter, statutory invention, industrial applicability (application), utility, enablement, support, clarity, written description, novelty, inventive step and nonobviousness since:
   (a) it is limited to a fragment of the protein that contains the binding pocket and was shown in the specification to retain binding activity and the signaling activity of the protein, and
   (b) the prior art does not teach any polypeptide which consists of the claimed specific part of the protein, or methods to specify parts of the polypeptide, and
   (c) it shows a significantly higher signaling activity compared to the whole protein.

6. The claim for:

(1) compounds in general identified by *in silico* screening methods

does not comply with enablement, support, clarity, and/or written description

7. In a case where the description gives no working examples of identifying compounds using the atomic coordinates of the protein, and the difference between the prior art and the claimed invention as a whole is limited to atomic coordinates stored on or employed by a machine, the claim for:

(1) *in silico* screening method

does not comply with one or more of the requirements of patent eligible subject matter, statutory invention, industrial applicability (application), utility, enablement, support, clarity, written description, novelty, inventive step and/or nonobviousness.

8. The claim for:

(1) compounds or their salts in general defined by a pharmacophore

does not comply with one or more of the requirements of enablement, support, clarity, and/or written description because

(a) it would require a trial and error effort beyond what is expected of a person having ordinary skill in the art to envisage a ligand structure other than the one described concretely in the examples, and make such compounds, and

(b) the pharmacophore, which is an abstract concept, does not define a compound.