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Application No.	Ref.	Date
99 916 262.1 - 2201	CST/P71576EP	17.03.2006
Applicant Triangle Pharmaceuticals Inc.		

Decision to refuse a European Patent application

The Examining Division - at the oral proceedings dated 28.02.2006 - has decided:

European Patent application No. 99 916 262.1 is refused.

Applicant/s:
Triangle Pharmaceuticals Inc.
4 University Place,
4611 University Drive
Durham, NC 27707
US

Title
SYSTEMS, METHODS AND COMPUTER PROGRAM PRODUCTS FOR GUIDING THE SELECTION OF THERAPEUTIC TREATMENT REGIMENS

The grounds for the decision are set out on the supplemental sheets annexed hereto.

Possibility of appeal

This decision is open to appeal.
Attention is drawn to the attached text of Articles 106 to 108 EPC.

Registered letter with advice of delivery

Examining Division:

Chairman:	Barba, M
2nd Examiner:	Sisk, A
1st Examiner:	Chabros, C

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Enclosure(s): 9 page/s reasons (Form 2916)
Form 2019

to EPO postal service: 14.03.06

Registered letter with advice of delivery
EPO Form 2007 05.98CSX

I. Summary of Facts and Submissions

1. The Euro-PCT patent application no. 99916262.1 is based on the international patent application PCT/US9907171, published under the number WO 99/52025 on 14.10.1999. This Euro-PCT application was filed with entry of the above mentioned international patent application into regional phase before the EPO on 3.11.2000. The bibliographic data of the application was published on the 17.01.2001 with the European publication number 1068568.

2. The following documents (D1-D5) were cited by the examining division in the procedure:

   D1: LANGLOTZ et al., "Adapting a consultation system to critique user plans", Int. J. Man-Machine Studies, Vol. 19, 1983, pages 479-496
   D2: PAZZANI et al., "Application of an Expert System in the Management of HIV-Infected Patients", JOURNAL OF ACQUIRED IMMUNE DEFICIENCY SYNDROMES AND HUMAN RETROVIROLOGY, Vol. 15, No. 5, 1997, pages 356-362
   D3: SIEPMANN, BACHMANN, "HTN-APT: Computer Aid in Hypertension Management", The Journal of Family Practice, Vol. 24, No. 3, 1987, pages 313-316
   D4: US 4 839 822 A
   D5: "OVERSEER: A Prototype Expert System for Monitoring Drug Treatment in the Psychiatric Clinic"; JOSEPH D. BRONZINO, RALPH A. MORELLI, JOHN W. GOETHE; IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING, VOL. 36, NO. 5. MAY 1989

   Documents D1-D4 were cited in the Supplementary European Search Report. Document D5 was introduced with the summons to attend oral proceedings according to the Guidelines, C-VI, 8.7.

3. In the communication of 9.03.2005, the applicant was advised that the subject matter of claim 1 does not meet the requirements of Article 56 EPC.

4. As a response, the applicant filed with letter of 5.09.2005 three new sets of claims (Main Request, First Auxiliary Request and Second Auxiliary Request) and amended pages of the description 4-5.

5. The applicant requested the grant of a patent based on the following documents:

Main Request

Description, Pages				
1-3, 6-39	as originally filed			
4, 5	received on	12.09.2005	with letter of	05.09.2005
Claims, Numbers				
1-23	received on	12.09.2005	with letter of	05.09.2005
Drawings, Sheets				
1/22-22/22	as originally filed			

First Auxiliary Request

Description, Pages				
1-3, 6-39	as originally filed			
4, 5	received on	12.09.2005	with letter of	05.09.2005
Claims, Numbers				
1-22	received on	12.09.2005	with letter of	05.09.2005
Drawings, Sheets				
1/22-22/22	as originally filed			

Second Auxiliary Request

Description, Pages				
1-3, 6-39	as originally filed			
4, 5	received on	12.09.2005	with letter of	05.09.2005
Claims, Numbers				
1-21	received on	12.09.2005	with letter of	05.09.2005

Drawings, Sheets
1/22-22/22 as originally filed

6. In this version of the claims, the applicant has drafted claim 1 using the two part form as specified in Rule 29 (1) EPC, whereby the only features inserted in the characterising portion are the ones related to the step of:

   evaluating patient information when new patient information is provided, and providing an **alert** according to a result of said evaluation when said patient information is contraindicated with or antagonistic of the patient's current therapeutic treatment regimen.

7. The applicant was summoned to attend oral proceedings with letter of 27.10.2005.
8. Oral proceedings were held on 28.02.2006 without the presence of any representative of the applicants.

II. Reasons for the Decision

10. **MAIN REQUEST:**

10.1 The present application does not meet the requirements of Article 52(1) EPC, because the subject-matter of claim 1, main request, does not involve an inventive step in the sense of Article 56 EPC.

10.2 As already mentioned by the examining division in it's communication of 9.03.2005, the features present in the preamble are disclosed by the combination of the methods known from the combination of documents D1 and D2.

With regard to the features inserted in the characterising portion of claim 1, these are also considered known in the art as they are disclosed in document D5 as was specified in the summons to oral proceedings.

The examining division is aware of the fact that it is not considered usual practice in order to dispute inventive step to combine more than two documents. However, as

described in the Guidelines G-C IV-9.9, the combination of more than two documents is admitted in special circumstances, as the presence of a plurality of features solving technical problems which are not synergistically related.

Therefore, the subject matter of present claim 1 of Main Request is not considered inventive against the combination of the methods known from documents D1, D2 and D5.

10.3 The document D1 is regarded as the closest prior art to the subject-matter of claim 1, as discussed in the communication of 9 March 2005.

Three sets of features constituting differences between the subject-matter of claim 1 and the closest prior art (sets of distiguishing features) are identified.

The **first set of distinguishing features** remains as identified in the communication of 9 March 2005 under point 2.2, subparagraph 1:
- three knowledge bases comprising information from different knowledge domains are used in the method (instead of one).

The **second set of distinguishing features** remains as identified in the communication of 9 March 2005 under point 2.2, subparagraph 2:
- a **ranked listing** of recommended treatment regimens is generated by the method.

The following **third set of distingushing features** was introduced with the letter of 5 September 2005:

- the method **evaluates** patient information when new patient information is provided and provides an **alert** according to a result of said evaluation when said patient information is contraindicated with or antagonistic of the patient's current therapeutic treatment regimen.

10.4 However, no technical effect is achieved by all the distinguishing features taken in combination. Rather, a plurality of partial problems is independently solved by the different sets of distinguishing features (see G-C-IV 9.8.2). The above identified sets

of distinguishing features constitute a simple aggregation, without giving a combined, synergistic technical effect (see G-C-IV 9.5).

10.5 The technical effect provided by the first set of distinguishing features is supplying the expert system with a multiplicity of domain specific knowledge bases. It is noted that in the application as a whole no effect related to the fact that the knowledge at the disposal of the rule-based expert system is partitioned among a **plurality** of knowledge bases is defined. Only the naming of the knowledge bases (in the claims, description and drawings), i.e. the characterisation of the knowledge bases by the content of the rules implies that placing of multiple knowledge bases merely reflects the the pre-existing division of their content.

The **first partial technical problem** can be formulated as the improved manageability of the knowledge bases (see communication of 9 March 2005, point 2.2). In fact, a professional in one of the specified knowledge domains (e.g. advisory information) would have a better manageability of a knowledge base containing only rules relating to the domain he is responsible of. This professional would not have to pre-select the rules he would like to modify in order to restrict himself to his own domain and he would not have to constantly monitor that he is not changing rules of other knowledges domains of which he is not responsible.

However, the usage of multiple knowledge databases for storing information relating to different knowledge domains for the use of an expert system would be considered by the skilled person. It is a common design principle in the field of expert systems and lies within the common general knowledge and custom of practice in this field. It thus doesn't confer inventive character to the subject-matter of the application.

10.6 The technical effect provided by the second set of distinguishing features is the provision of a ranked choice of recommended therapeutic treatment regimens, which is relevant or especially beneficial in cases where multiple regimen possibilities are legitimate.

The **second partial technical problem** based on the disclosure of D1 might

therefore be formulated as to provide to a physician a broader choice of recommended treatment regimens.

The person skilled in the art, faced with this problem, would take account of the concept disclosed in document D2 of suggesting the physician a ranked list of recommended regimens.

D2 discloses an expert system for regimen recommendation based on information in the medical literature and patient laboratory data (see abstract). It shares with the method of claim 1 the technical methodology (rule based expert system), the field of application (medicine) and the objective (regimen recommendation). Moreover, the system of D2 is applied in a domain where the above formulated technical problem is valid.

The similarities in D2 form an obvious indicator for the skilled person to apply the concept of a ranked list of recommended regimens to the method of D1, thereby arriving at the same solution as defined in claim 1.

10.7 The technical effect provided by the third set of distinguishing features is the ability of the system to provide timely and critical alerts with potentially life saving consequences .

The **third partial technical problem** underlying this technical effect is the provision of a treatment monitoring functionality to the treatment consultation and critiquing system of D1.

D5 discloses an expert system that monitors the drug treatment of patients in real time. The system issues alerts when standard clinical practices are not followed or when laboratory results are abnormal. The system utilizes all available pharmacy and laboratory data (see abstract). Contraindication conditions with current therapeutic treatment regimens are an example of alerts (see p.535, left column, line 5).

Moreover, the departure point of establishing the design criteria for the drug therapy

monitoring system of D5 were also therapy recommendation systems/methods, like the part of the method of claim 1 which is defined in the preamble. The authors analyse why current therapy recommendation systems did not gain acceptance among practising clinicians. They identify that an important reason for this is that they are "too tedious to work with and tend to 'seize control' of the decision making process from the clinician" (p. 534, left column, 1st para). To address this problem, the authors decide to build a knowledge-based system that "does not require extensive interaction by the clinical staff and does not encroach in any way on the clinician's decision-making responsibility". Therefore, they propose a "monitoring system, reporting apparent instances of 'inappropriate' treatment, and not an advisory system" (p.534, para "Design Considerations").

This teaching of D5 would prompt the person skilled in the art to combine the advantages of both kinds of systems, the therapy recommendation system and the therapy monitoring system, in order to increase the available functionality of a clinical decision support system.

Therefore, the person skilled in the art, confronted with the above identified third partial technical problem, would use the teaching of document D5 to **evaluate** patient information when new patient information is provided and provide **alerts** according to a result of said evaluation when said patient information is contraindicated with or antagonistic of the patient's current therapeutic treatment regimen.

10.8 No combined technical effect of the three sets of distinguishing features is implied by the application as whole nor can be otherwise identified.

E.g. a method using multiple knowledge bases serving different knowledge domains would seem to provide an identical ranked listing of recommended treatment regimens as a method using a single knowledge base storing information from the various knowledge domains. The application does not give any details as to how the different knowledge bases are technically separated. Therefore, they are perfectly equivalent for the generation of the ranked listing of recommended treatment regimens. Hence, there is no synergistic effect between the first and the second set

of distinguishing features.
The same applies for the evaluation of new patient information and generation of alerts versus the existence of a single/a multiplicity of knowledge bases.
Also, no combinatorial effect is apparent between the step of producing a ranked listing of therapeutic treatment regimens and the evaluation of new patient information and generation of alerts.

10.9 Consequently, the skilled person, confronted with the partial technical problems as formulated above, would arrive, without the exercise of inventive skill, at a solution falling within the scope of claim 1 Main Request.

Consequently, claim 1 of the Main Request lacks an inventive step.

11. FIRST AND SECOND AUXILIARY REQUESTS:

11.1 The present application does not meet the requirements of Article 52(1) EPC, because the subject-matter of claims 1 in the First Auxiliary Request and the Second Auxiliary Request does not involve an inventive step in the sense of Article 56 EPC.

11.2 The document D1 is regarded as the closest prior art to the subject-matter of claim 1 First Auxiliary Request.

The following features are added to the subject-matter of claim 1 First Auxiliary Request, compared to claim 1 Main Request:

- the patient information includes laboratory data and assessment data, and the step of **evaluating** said patient information comprises the step of determining **whether the laboratory data and assessment data are too old to be considered reliable**.

This feature reflects only the informational content of rules stored in the knowledge base and the facts on which the rules draw on. The content of the rules, or other type of knowledge (e.g. premises, conclusions) processed by the expert system is

not of technical, but of medical nature. Hence this feature cannot contribute to the technical character of the invention (see G-C-IV 9.8.2). Consequently, claim 1 First Auxiliary Request is not inventive over the prior art.

Notwithstanding this argumentation, it is pointed out that the method of D5 also discloses that the patient data includes laboratory data (see abstract) and assessment data (diagnostic data, see p.535, left column).

11.3 The following features are added to the subject-matter of claim 1 Second Auxiliary Request, compared to claim 1 First Auxiliary Request:

- steps (b) and (c) are repeated when new patient information is provided.

These features are considered obvious over the disclosure of D1 in light of the disclosure of D5. The technical problem remains the same as defined under point 10.7 above. Following the argumentation of point 10.7, the teaching of D5 would prompt the skilled person to combine the advantages of both kinds of systems in order to increase the available functionality of a clinical decision support system. A reevaluation of the proposed treatment regimens and advisory information after new patient has been analysed (i.e. steps (b) and (c)) would be an obvious and straightforward design choice for the skilled person combining both systems.

Consequently, claim 1 of the Second Auxiliary Request lacks inventive character.

12. Since the application does not meet the requirements of the EPC, the application is refused (Article 97(1) EPC).

Article 106
Decisions subject to appeal

(1) An appeal shall lie from decisions of the Receiving Section, Examining Divisions, Opposition Divisions and the Legal Division. It shall have suspensive effect.

(2) An appeal may be filed against the decisions of the Opposition Division even if the European patent has been surrendered or has lapsed for all the designated States.

(3) A decision which does not terminate proceedings as regards one of the parties can only be appealed together with the final decision, unless the decision allows separate appeal

(4) The apportionment of costs of opposition proceedings cannot be the sole subject of an appeal.

(5) A decision fixing the amount of costs of opposition proceedings cannot be appealed unless the amount is in excess of that laid down in the Rules relating to Fees.

Article 107
Persons entitled to appeal and to be parties to appeal proceedings

Any party to proceedings adversely affected by a decision may appeal. Any other parties to the proceedings shall be parties to the appeal proceedings as of right.

Article 108
Time limit and form of appeal

Notice of appeal must be filed in writing at the European Patent Office within **two months** after the date of notification of the decision appealed from. The notice shall not be deemed to have been filed until after the fee for appeal has been paid. Within **four months** after the date of notification of the decision, a written statement setting out the grounds of appeal must be filed.

Further information concerning the filing of an appeal

(a) The appeal is to be filed with the European Patent Office either at its seat in Munich, at its branch at The Hague or at its Berlin sub-office. The postal addresses are as follows:

(i) European Patent Office
D-80298 Munich
Germany
(Telex: 523656 epmu d)
(Fax: +49 89 2399-4465)

(ii) European Patent Office
Branch at The Hague
Patentlaan 2
Postbus 5818
NL-2280 HV Rijswijk (ZH)
Netherlands
(Telex: 31651 epo nl)
(Fax: +31 70 340-3016)

(iii) European Patent Office
Berlin sub-office
D-10958 Berlin
Germany
(Fax: +49 30 25901-840)

(b) The notice of appeal must contain the name and address of the appellant in accordance with the provisions of Rule 26(2)(c) EPC, and a **statement** identifying the decision which is impugned and the extent to which amendment or cancellation of the decision is requested (see Rule 64 EPC). The notice of appeal and any subsequent submissions stating the grounds for appeal must be signed.

(c) Notice of appeal must be **filed in writing** (typewritten or printed (Rule 36(2) EPC), by telegram, telex or fax (Rule 36(5) EPC; OJ EPO 6/89, 219-225; OJ EPO 9/89, 396)).

(d) The fee for appeal is laid down in the Rules relating to Fees. The equivalents in the national currencies in which the fee for appeal can be paid are regularly published in the Official Journal of the European Patent Office under the heading "Guidance for the payment of fees, costs and prices".