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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

(Also referred to as FORM PTO-1465)

REQUEST FOR *EX PARTE* REEXAMINATION TRANSMITTAL FORM

Address to:
Mail Stop *Ex Parte* Reexam
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Attorney Docket No.:

Date: February 25, 2004

1. ☑ This is a request for *ex parte* reexamination pursuant to 37 CFR 1.510 of patent number 6,455,275 issued September 24, 2002. The request is made by:

   ☐ patent owner. ☑ third party requester.

2. ☑ The name and address of the person requesting reexamination is:

   Daniel B. Ravicher, Executive Director

   Public Patent Foundation, Inc.

   404 W 51st St., # 3A, New York, NY 10019

3. ☐ a. A check in the amount of $_____ is enclosed to cover the reexamination fee, 37 CFR 1.20(c)(1);

   ☐ b. The Director is hereby authorized to charge the fee as set forth in 37 CFR 1.20(c)(1) to Deposit Account No. _____; or

   ☑ c. Payment by credit card. Form PTO-2038 is attached.

4. ☑ Any refund should be made by ☐ check or ☐ credit to Deposit ~~Account No.~~ _____. 37 CFR 1.26(c). If payment is made by credit card, refund must be to credit card account.

5. ☑ A copy of the patent to be reexamined having a double column format on one side of a separate paper is enclosed. 37 CFR 1.510(b)(4)

6. ☐ CD-ROM or CD-R in duplicate, Computer Program (Appendix) or large table

7. ☐ Nucleotide and/or Amino Acid Sequence Submission
   If applicable, all of the following are necessary.

   a. ☐ Computer Readable Form (CRF)
   b. Specification Sequence Listing on:

      i ☐ CD-ROM (2 copies) or CD-R (2 copies); **or**
      ii. ☐ paper

   c. ☐ Statements verifying identity of above copies

8. ☑ A copy of any disclaimer, certificate of correction or reexamination certificate issued in the patent is included.

9. ☑ Reexamination of claim(s) 1 to 20 is requested.

10. ☑ A copy of every patent or printed publication relied upon is submitted herewith including a listing thereof on Form PTO-1449 or equivalent.

11. ☑ An English language translation of all necessary and pertinent non-English language patents and/or printed publications is included.

12. ☑ The attached detailed request includes at least the following items:

a. A statement identifying each substantial new question of patentability based on prior patents and printed publications. 37 CFR 1.510(b)(1)
b. An identification of every claim for which reexamination is requested, and a detailed explanation of the pertinency and manner of applying the cited art to every claim for which reexamination is requested. 37 CFR 1.510(b)(2)

13. ☐ A proposed amendment is included (only where the patent owner is the requester). 37 CFR 1.510(e)

14. ☑ a. It is certified that a copy of this request (if filed by other than the patent owner) has been served in its entirety on the patent owner as provided in 37 CFR 1.33(c).
The name and address of the party served and the date of service are:
John P. White
Cooper and Dunham LLP
1185 Sixth Ave., New York, NY 10036
Date of Service: February 25, 2004; or

☐ b. A duplicate copy is enclosed since service on patent owner was not possible.

15. Correspondence Address: Direct all communication about the reexamination to:

☐ Customer Number:

OR

☑ Firm or Individual Name	Public Patent Foundation				
Address (line 1)	404 W 51st St., # 3A				
Address (line 2)					
City	New York	State	NY	Zip	10019
Country	USA				
Telephone	(917) 843-3425	Fax	(212) 977-9677		

16. ☑ The patent is currently the subject of the following concurrent proceeding(s):
☐ a. Copending reissue Application No. _____.
☐ b. Copending reexamination Control No. _____.
☐ c. Copending Interference No. _____.
☑ d. Copending litigation styled:
Biogen, Inc. et al v. Trustees of Columbia University, 03-11329 (Mass); Wyeth et al v. Trustees of Columbia University, 03-11570 (Mass); Baxter Healthcare Corp. v. Trustees of Columbia University, 03-12221 (Mass); (cont. at * below)

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

Authorized Signature	2/25/04 *Date*	
Daniel B. Ravicher, Esq. *Typed/Printed Name*	47,015 *Registration No., if applicable*	☐ *For Patent Owner Requester* ☑ *For Third Party Requester*

* Genentech Inc. v. Trustees of Columbia University, 03-01603 (N.Cal); Trustees of Columbia University v. Johnson & Johnson et al, 03-04875 (N.Cal); Immunex Corp., et al v. Trustees of Columbia University, 03-04349 (C.Cal); Sereno, Inc. et al v. Trustees of Columbia University, 03-12401 (Mass); and Johnson & Johnson v. Trustees of Columbia, 03-8811 (SDNY).

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE PATENT OF:	:	
AXEL ET AL.	:	EXAMINER:
PATENT NO. 6,455,275	:	
(ISSUED SEPTEMBER 24, 2002)	:	
SERIAL NO. 08/484,136	:	GROUP ART UNIT:
(FILED JUNE 7, 1995)	:	

FOR: DNA CONSTRUCT FOR PRODUCING PROTEINACEOUS MATERIALS IN EUCARYOTIC CELLS

EX PARTE REQUEST FOR REEXAMINATION OF A PATENT UNDER 37 C.F.R. § 1.510

MAIL STOP *EX PARTE* REEXAM
COMMISSIONER FOR PATENTS
P.O. BOX 1450
ALEXANDRIA, VA 22313-1450

SIR:

The Public Patent Foundation respectfully requests that claims 1 to 20 of United States Patent No. 6,455,275 to Axel et al. be reexamined ex parte.

The requirements set forth in 37 C.F.R. § 1.510 are fulfilled as follows:

I. 37 C.F.R. § 1.510(a)

The $2,520 fee specified in 37 C.F.R. § 1.20(c) may be charged to the credit card set forth on the enclosed Credit Card Payment Form.

II. 37 C.F.R. § 1.510(b) – Required Contents of Request

A. 37 C.F.R. § 1.510(b)(1) – A Statement Pointing Out Each Substantial New Question of Patentability Based Upon Prior Patents and Printed Publications

The substantial new question of patentability raised by this request is whether each of the claims 1 to 20 of U.S. Patent No 6,455,275 ("'275 patent") to Axel et al. is unpatentable for double patenting in view of Axel et al.'s prior U.S. Patents Nos. 4,399,216, 4,634,665, and 5,179,017 ("'216 patent", "'665 patent", and "'017 patent", respectively; "Prior Axel Patents", collectively).

B. 37 C.F.R. § 1.510(b)(2) – Identification of Every Claim for Which Reexamination is Requested and a Detailed Explanation of the Pertinency and Manner of Applying the Cited Prior Patents to the '275 Patent Claims

Reexamination is requested for all 20 of the '275 patent's claims. A detailed explanation of the pertinency of the Prior Axel Patents and the manner of applying the Prior Axel Patents to the '275 patent's claims is set forth below under the heading Detailed Explanation.

C. 37 C.F.R. § 1.510(b)(3) – A Copy of Every Patent and Printed Publication Relied Upon or Referred To

Each of the Prior Axel Patents is attached hereto as Appendix B, which also includes a listing thereof on Form PTO/SB/08A.

D. 37 C.F.R. § 1.510(b)(4) – A Copy of the Entire Patent for Which Reexamination is Requested

A copy of the '275 patent in double column format with each page plainly written on only one side of a sheet of paper is attached hereto as Appendix A.

E. 37 C.F.R. § 1.510(b)(5) – Certificate of Service on the Patent Owner at the Address Specified in 37 C.F.R. § 1.33(c)

As certified on the Transmittal Form, a copy of that form and this request, including all attachments, has been served in its entirety on John P. White, Cooper and Dunham LLP, 1185 Sixth Ave, New York NY US 10036.

III. Co-Pending Litigation

The '275 patent is currently involved in the following pending litigation:

- Genentech Inc. v. The Trustees of Columbia University of the City of New York, 3:03-cv-01603 (Northern District of California)
- Immunex Corp. and Amgen Inc. v. The Trustees of Columbia University in the City of New York, 2:03cv04349 (Central District of California)
- Biogen, Inc., Genzyme Corp. and Abbott Bioresearch Center v. The Trustees of Columbia University in the City of New York, 1:03-cv-11329-MLW (District of Massachusetts)
- Wyeth and Genetics Institute LLC v. The Trustees of Columbia University in the City of New York, 1:03-cv-11570-MLW (District of Massachusetts)
- The Trustees of Columbia University in the City of New York v. Johnson & Johnson and Ares Trading S.A., 3:03-cv-04875-PJH (Northern District of California)
- Johnson & Johnson v. Trustees of Columbia University City of NY, 1:03-cv-08811-BSJ-KNF (Southern District of New York)
- Baxter Healthcare Corp. v. The Trustees of Columbia University in the City of New York, 1:03-cv-12221-MLW (District of Massachusetts)
- Sereno, Inc. and Ares trading S.A. v. The Trustees of Columbia University in the City of New York, 1:03-cv-12401-MLW (District of Massachusetts)

DETAILED EXPLANATION

Introduction

The Public Patent Foundation ("PUBPAT") is a not-for-profit corporation that aims to protect the public from the harms caused by wrongly issued patents and unsound patent policy. PUBPAT provides the general public, particularly those persons or businesses otherwise deprived of access to the system governing patents, with representation, advocacy, and education. PUBPAT submits this request for ex parte reexamination of all 20 claims of U.S. Patent No 6,455,275 ("'275 patent") to Axel et al. because they are each invalid for double patenting in light of three previous patents granted to Axel et al., namely U.S. Patents Nos. 4,399,216, 4,634,665, and 5,179,017 ("'216 patent", "'665 patent", and "'017 patent", respectively; "Prior Axel Patents", collectively).

The '275 patent claims Chinese Hamster Ovary ("CHO") cells used in a process for producing proteinaceous material. It issued in September 2002, more than twenty-two years after the February 1980 filing of the original application to which it claims priority. Over the course of those twenty-two years, Axel et al. filed a string of nine related applications, all of which contained virtually identical disclosures, and received the three Prior Axel Patents, all of which expired in August 2000, in addition to the '275 patent, which will not expire until September 2019.

None of Axel et al.'s four patents are patentably distinct from one another. The first two Prior Axel Patents, the '216 patent and the '665 patent, claim a process that results in a transformed cell in which foreign DNA has been incorporated. The third Prior Axel Patent, the '017 patent, and the '275 patent claim the transformed cell that results from that process. Axel et al. conceded that the Prior Axel Patents were not patentably distinct from one another by

entering terminal disclaimers in response to double patenting rejections of the applications leading to the second and third Prior Axel Patents without even so much as an argument. Unfortunately, the three Prior Axel Patents, and the hundreds of millions of dollars Axel et al. made in licensing them, was not enough to satisfy Axel et al.'s desire for more patents and more money.[1]

In an attempt to get a second pound of flesh from the American public, on June 7, 1995, Axel et al. filed the ninth application claiming priority from the same 1980 original application on which each of the Prior Axel Patents was based.[2] The Examiner repeatedly rejected this application for double patenting in light of the Prior Axel Patents, just as the applications leading to the '665 patent and the '017 patent had been rejected for double patenting. This time, however, Axel et al. did not concede the propriety of the rejection and enter a terminal disclaimer, because doing so would have destroyed any hope Axel et al. had of getting an extension of patent protection and licensing revenue beyond the expiration of the Prior Axel Patents. Eventually, after seven years of prosecution, which included unreasonable and unexplainable delay on the part of Axel et al. and changes in the personnel examining the application, the '275 patent was allowed. As set forth in more detail below, the '275 patent is invalid for double patenting in light of the Prior Axel Patents.

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[1] Pleadings filed in the co-pending litigations state that the assignee of the Axel et al. patents, The Trustees of Columbia University in the City of New York, has received hundreds of millions of dollars in licensing fees for the Prior Axel Patents and is seeking to extend the receipt of such royalties through the expiration of the '275 patent in 2019.

[2] The June 7, 1995 filing date was not random. If the application had been filed one day later, any resulting patent would have had a term under the new 20-years-from-application rule that took effect on June 8, 1995. Since Axel et al. beat, by one day, the effective date for the change in the law regarding the computation of patent term, it fell under the old regime of 17-years-from-issue. This difference of one day extends the term of the '275 patent by 17 years, because if it had issued under the new rule it would have expired in February 2000, twenty years from the filing date of its earliest priority application. Instead, Axel et al. made sure the application fell under the old law, so that any patent issued from it would have a term of 17 years from its issue.

If maintained, the '275 patent will enable Axel et al. to reap hundreds of millions of dollars from the American economy through licensing fees between now and 2019, when the '275 patent will otherwise expire. Even more troubling is that the technology claimed in the Prior Axel Patents and the '275 patent relates to the production of medically necessary products, such as Epogen® for anemia, Activase® for heart attacks and stroke, Avonex® for multiple sclerosis, and Recombinate® for hemophilia. PUBPAT is concerned that maintenance of the '275 patent will harm the public health because consumers will be forced to pay higher prices in order to compensate the distributors of these products for the royalties they must pass on to Axel et al.. These public health concerns are of paramount importance, and must be considered in determining whether to grant this request for ex parte reexamination of the '275 patent.

Axel et al. rightfully earned the three Prior Axel Patents and the hundreds of millions of dollars that resulted from their license, but the '275 patent and the additional hundreds of millions Axel et al. will reap from licensing it between now and when it would otherwise expire in 2019 are unmerited. As such, the '275 patent should be reexamined, and ultimately revoked in its entirety.

The Substantial New Question: Double Patenting

The substantial new question raised by this request is whether each of the '275 patent's 20 claims are invalid for double patenting in light of the Prior Axel Patents. Double patenting prevents a patentee from obtaining a time-wise extension of patent rights. In re Longi, 759 F.2d 887, 892 (Fed. Cir. 1985). There are two types of double patenting: (1) same invention and (2) obviousness-type. "Same invention" double patenting is based upon 35 U.S.C. § 101, which states that an inventor may obtain "a patent" for an invention, meaning that only one

patent may be granted for any single invention. The phrase "same invention" means an invention drawn to virtually identical subject matter.

"Obviousness-type" double patenting, on the other hand, is a judicially created doctrine that precludes an inventor from receiving a second patent with claims that are "not patentably distinct" from the claims of a prior patent to the same inventor. Id. Claims are unpatentable on the ground of obviousness-type double patenting if the additional limitations they contain over the claims in a prior patent to the same inventor are obvious. The determination of whether claims are obvious in light of prior claims issued to the same inventor under obviousness-type double patenting follows precisely the same analysis as for determining whether claims are obvious in light of prior art.

As set forth in more detail immediately below, the following chart identifies claims of the Prior Axel Patents that render each claim of the '275 patent invalid for double patenting. For the sake of efficiency, however, this is not an exhaustive list, and reexamination of the '275 patent should not be limited to just these basis of invalidity.

'275 Patent Claim	**Prior Axel Patents Claims**
1	'216: 73; '017: 2, 5
2	'216: 54; '017: 5
3	'216: 47; '017: 4
4	'216: 47; '017: 2, 4
5, 16, 18	'665: 12; '017: 2
6	'665: 11, 12; '017: 2
7, 8, 9	'665: 3, 12; '017: 2
10, 11, 12	'665: 2, 12; '017: 2
13, 19	'665: 12; '017: 2, 5
14, 15	'665: 12, 14; '017: 2
17	'665: 12; '017: 2, 4
20	'216: 70; '017: 4

Claims 1 and 2

Claims 1 and 2 of the '275 patent read as follows:

> 1. A transformed Chinese Hamster Ovary cell comprising a DNA construct comprising DNA I encoding a proteinaceous material foreign to the Chinese Hamster Ovary cell and linked thereto DNA II encoding an amplifiable dominant selectable phenotype not expressed by such Chinese Hamster Ovary cell prior to transformation with the construct, the construct being effective for producing the proteinaceous material when the construct is introduced into the Chinese Hamster Ovary cell, wherein the construct is stably incorporated into the chromosomal DNA of the transformed Chinese Hamster Ovary cell.
>
> 2. A method of producing a proteinaceous material which comprises culturing transformed Chinese Hamster Ovary cells according to claim 1 under suitable conditions to produce the proteinaceous material and recovering the proteinaceous material so produced.

Claim 1 of the '275 patent is invalid for double patenting in light of claim 73 of the '216 patent and claims 2 and 5 of the '017 patent, which read:

> '216, cl. 73. A mammalian cell into which foreign DNA I has been inserted in accordance with the process of claim 54. → 54. A process for generating a multiplicity of foregin DNA I molecules corresponding to multiple copies of a gene in a eucaryotic cell which comprises tranforming said eucaryotic cell with a molecule which is formed by linking one of said foreign DNA I molecules to a DNA II molecule corresponding to an amplifiable gene for a dominant selectable phenotype not expressed by said eucaryotic cell, and culturing the transformed eucaryotic cells in the presence of successively elevated concentrations of an agent permitting survival or identification of eucaryotic cells which have acquired multiple copies of said amplifiable gene, said transformation and culturing being carried out under suitable conditions.
>
> '017, cl. 2. The transferred Chinese Hamster Ovary cell of claim 1, wherein foreign DNA I encodes a proteinaceous material which is not associated with a selectable phenotype. → 1. A transformed Chinese Hamster Ovary cell which comprises amplified foreign DNA I corresponding to a gene of interest stably incorporated into the chromosomal DNA of the transformed cell and amplified DNA II encoding a dominant selectable phenotype not expressed by the transformed cell prior to transformation.

'017, cl. 5. A method of obtaining a proteinaceous protein which comprises culturing transformed cells in accordance with claim 1 under suitable conditions and recovering the proteinaceous material from the transformed cells so cultured. → 1. A transformed Chinese Hamster Ovary cell which comprises amplified foreign DNA I corresponding to a gene of interest stably incorporated into the chromosomal DNA of the transformed cell and amplified DNA II encoding a dominant selectable phenotype not expressed by the transformed cell prior to transformation.

The only substantive difference between claim 1 of the '275 patent and claim 73 of the '216 patent is that claim 73 of the '216 patent is more general, to "DNA molecules", than claim 1 of the '275 patent, which is limited to "proteinaceous material." Such a difference is not patentably distinct, however, as the Prior Axel Patents teach and claim using a cell that generates a multiplicity of DNA molecules to harvest protein. For example, claim 2 of the '017 patent expressly claims "proteinaceous material" and claim 5 of the '017 patent expressly claims harvesting protein from a transformed CHO cell. Although claim 5 of the '017 patent is not a product claim like claim 1 of the '275 patent, it nevertheless discloses a product to which claim 1 of the '275 patent is virtually identical or from which claim 1 of the '275 patent is not patentably distinct.

The other differences between claim 1 of the '275 patent and the cited claims of the Prior Axel Patents also do not render it patentably distinct. The CHO cell of claim 1 of the '275 patent is a type of the mammalian cell claimed in claim 73 of the '216 patent. The phrase "DNA construct" in claim 1 of the '275 patent is simply an added term indicating that the linked DNA molecules were humanly created, not naturally occurring. Such an added term creates no patentably distinct difference, as the cited claims of the Prior Axel Patents are also directed to humanly created, not naturally occurring, "foreign" DNA molecules.

Further, the phrase "being stably incorporated" in claim 1 of the '275 patent means the same as the language "carried out under suitable conditions ... permitting survival"

found in claim 73 of the '216 patent. The difference in language creates no patentably distinct difference. Therefore, claim 1 of the '275 patent is virtually identical to or not patentably distinct from either claim 73 of the '216 patent, claims 2 or 5 of the '017 patent, or claim 73 of the '216 patent in light of claims 2 and 5 of the '017 patent.

During prosecution of the '275 patent, Axel et al. argued that none of the claims of the '216 patent make obvious the "linked" limitation in claim 1 of the '275 patent. Amendment, February 12, 2002. However, that is just simply not accurate. Claim 54 of the '216 patent, from which claim 73 depends, expressly recites "linking one of said foreign DNA I molecules to a DNA II molecule." Further, claims 2 and 5 of the '017 patent depend from claim 1 of the '017 patent, which is not limited to either linked or unlinked DNA II. Therefore, they claim both.

Claim 2 of the '275 patent is invalid for double patenting in light of claim 5 of the '017 patent (set forth above with respect to claim 1) and claim 54 of the '216 patent, which reads:

> '216, cl. 54. A process for generating a multiplicity of foregin DNA I molecules corresponding to multiple copies of a gene in a eucaryotic cell which comprises tranforming said eucaryotic cell with a molecule which is formed by linking one of said foreign DNA I molecules to a DNA II molecule corresponding to an amplifiable gene for a dominant selectable phenotype not expressed by said eucaryotic cell, and culturing the transformed eucaryotic cells in the presence of successively elevated concentrations of an agent permitting survival or identification of eucaryotic cells which have acquired multiple copies of said amplifiable gene, said transformation and culturing being carried out under suitable conditions.

There are no differences between claim 2 of the '275 patent and claim 5 of the '017 patent other than those discussed above with respect to claim 1 of the '275 patent. Therefore, claim 2 of the '275 patent is virtually identical to or not patentably distinct from claim 5 of the '017 patent.

Further, since claim 2 of the '275 patent is simply a method claim based on the product claim of claim 1 of the '275 patent, and since claim 54 of the '216 patent is the method

claim on which the product claim of claim 73 of the '216 patent is based, claim 2 of the '2175 patent is virtually identical to or not patentably distinct from claim 54 of the '216 patent for the same reasons that claim 1 of the '275 patent is virtually identical to or not patentably distinct from claim 73 of the '216 patent.

Claims 3 and 4

Claims 3 and 4 of the '275 patent read as follows:

> 3. A transformed Chinese Hamster Ovary (CHO) cell which comprises amplified foreign DNA I encoding a proteinaceous material and amplified DNA II encoding a dihydrofolate reductase not expressed by the transformed CHO cell prior to transformation, both DNA I and DNA II being stably incorporated into the chromosomal DNA of the transformed CHO cell.
>
> 4. The transformed Chinese Hamster Ovary cell of claim 3, wherein the proteinaceous material is a glycoprotein.

Claim 3 of the '275 patent is invalid for double patenting in light of claim 47 of the '216 patent and claim 4 of the '017 patent, which read:

> '216, cl. 47. A process in accordance with claim 46 wherein said gene associated with drug resistance is a gene coding for a mutant dihydrofolate reductase which renders cells resistant to methotrexate. → 46. A process in accordance with claim 31 wherein said foreign DNA II which does for proteinaceous material which is associated with a selectable phenotype comprises a gene associated with drug resistance. → 31. A process for inserting a multiplicity of foreign DNA I molecules corresponding to multiple copies of a gene coding for a proteinaceous material into a suitable eucaryotic cell which comprises cotransforming said eucaryotic cell with said multiplicity of foreign DNA I molecules and with a multiplicity of unlinked foreign DNA II molecules coding for a selectable phenotype not expressed by said eucaryotic cell, said cotransformation being carried out under suitable conditions permitting survival or identification of eucaryotic cells which have acquired said multiplicity of genes coding for said selectable phenotype.
>
> '017, cl. 4. The transferred Chinese Hamster Ovary cell of claim 1, wherein DNA II encodes a dihydrofolate reductase which renders the transformed cell resistant to methotrexate. → 1. A transformed

> Chinese Hamster Ovary cell which comprises amplified foreign DNA I corresponding to a gene of interest stably incorporated into the chromosomal DNA of the transformed cell and amplified DNA II encoding a dominant selectable phenotype not expressed by the transformed cell prior to transformation.

The only difference between claim 3 of the '275 patent and claim 4 of the '017 patent is that claim 3 of the '275 patent is limited to "DNA I encoding a proteinaceous material" while claim 4 of the '017 patent is limited to "DNA I corresponding to a gene of interest." However, "DNA I encoding a proteinaceous material" is inherent or obvious in light of a Prior Axel Patents claim reciting "DNA I corresponding to a gene of interest," especially since the Prior Axel Patents extensively teach and claim DNA I encoding a proteinaceous material. For example, claim 2 of the '017 patent expressly recites such a limitation.

Further, although claim 47 of the '216 patent is not a product claim like claim 3 of the '275 patent, it nevertheless discloses a product to which the product of claim 3 of the '275 patent is virtually identical or from which the product of claim 3 of the '275 patent is not patentably distinct. Therefore, claim 3 of the '275 patent is virtually identical to or not patentably distinct from either claim 47 of the '216 patent, claim 4 of the '017 patent, or claim 47 of the '216 patent in light of claim 4 of the '017 patent.

Axel et al. argued during prosecution of the '275 patent that claim 3 of the '275 patent was unobvious over the Prior Axel Patents because of the recitation that both DNA I and DNA II are amplified. Amendment, February 12, 2002. DNA amplification simply means creating copies of DNA, such as is claimed in claim 47 of the '216 patent, which states "a multiplicity of ... DNA II." Regardless, claim 4 of the '017 patent expressly claims "amplified ... DNA I" in combination with "amplified DNA II." Therefore, both claim 47 of the '216 patent and claim 4 of the '017 patent contain the limitation in claim 3 of the '275 patent that both DNA I and DNA II are amplified.

Claim 4 of the '275 patent is invalid for double patenting in light of claim 47 of the '216 patent and claim 4 of the '017 patent (both set forth above with respect to claim 3) and claim 2 of the '017 patent, which reads:

> '017, cl. 2. The transferred Chinese Hamster Ovary cell of claim 1, wherein foreign DNA I encodes a proteinaceous material which is not associated with a selectable phenotype. → 1. A transformed Chinese Hamster Ovary cell which comprises amplified foreign DNA I corresponding to a gene of interest stably incorporated into the chromosomal DNA of the transformed cell and amplified DNA II encoding a dominant selectable phenotype not expressed by the transformed cell prior to transformation.

Claim 4 of the '275 patent depends from claim 3 of the '275 patent and adds only a limitation that "the proteinaceous material is a glycoprotein." Glycoprotein is discussed throughout the specification of each of the Prior Axel Patents as being an example, if not a targeted, proteinaceous material appropriate for the invention claimed in the Prior Axel Patents. See, e.g., '216 patent, col. 3, lines 14-18 ("[i]t is therefore another important object of this invention to provide a process for producing compounds which include ... proteinaceous moieties such as glycoproteins"); '216 patent, col. 6, lines 39-43 ("the invention provides a process for producing ... proteinaceous products such as the glycoproteins").

Therefore, the claims of the Prior Axel Patents directed to a CHO cell encoding a proteinaceous material, such as claim 2 of the '017 patent, inherently claim or render obvious a CHO cell encoding a glycoprotein as claimed in claim 4 of the '275 patent. As such, claim 4 of the '275 patent is virtually identical to or not patentably distinct from claim 4 of the '017 patent in light of claim 47 of the '216 patent and claim 2 of the '017 patent.

Claims 5 and 6

Claims 5 and 6 of the '275 patent read as follows:

> 5. A transformed Chinese Hamster Ovary (CHO) cell which comprises amplified foreign DNA I corresponding to a gene of

> interest which encodes a proteinaceous material and amplified DNA II encoding a dominant selectable phenotype not expressed by the transformed cell prior to transformation, DNA I or DNA II or both being attached to bacterial plasmid DNA or phage DNA, and both DNA I and DNA II being stably incorporated into the chromosomal DNA of the transformed cell.
>
> 6. The transformed CHO cell of claim 5, wherein DNA II encodes a dihydrofolate reductase which renders the transformed CHO cell resistant to methotrexate.

Claim 5 of the '275 patent is invalid for double patenting in light of claim 12 of the '665 patent and claim 2 of the '017 patent, which read:

> '665, cl. 12. A eucaryotic cell into which foreign DNA I has been inserted in accordance with the process of claim 1. → 1. A process for inserting foreign DNA I into a suitable eucaryotic cell which comprises cotransforming said eucaryotic cell with said foreign DNA I and with unlinked foreign DNA II which codes for a selectable phenotype not expressed by said eucaryotic cell, said cotransformation being carried out under suitable conditions permitting survival or identification of eucaryotic cells which have acquired said selectable phenotype, said foreign DNA II being attached to bacterial plasmid or phage DNA.
>
> '017, cl. 2. The transferred Chinese Hamster Ovary cell of claim 1, wherein foreign DNA I encodes a proteinaceous material which is not associated with a selectable phenotype. → 1. A transformed Chinese Hamster Ovary cell which comprises amplified foreign DNA I corresponding to a gene of interest stably incorporated into the chromosomal DNA of the transformed cell and amplified DNA II encoding a dominant selectable phenotype not expressed by the transformed cell prior to transformation.

The only difference between claim 5 of the '275 patent and claim 12 of the '665 patent is an express statement that the DNA II is amplified. In fact, Axel et al. argued in the prosecution history of the '275 patent that claim 5 of the '275 patent was unobvious over the Prior Axel Patents because of it expressly contained the combination of "bacterial plasmid DNA or phage DNA" and "amplified DNA II" limitations. Amendment, February 12, 2002. However, claim 12 of the '665 patent expressly recites the limitation of "permitting survival and identification

of" cells which "have acquired" the selectable phenotype coded by the DNA II. It is inherent in a cell which "survives" and "can be identified as having acquired a selectable phenotype coded by DNA II" that the DNA II will be copied. Such copying is amplification. Therefore, claim 12 of the '665 inherently discloses amplified DNA II.

Further, the Prior Axel Patents extensively teach and claim amplified DNA II as part of the invention. For example, Claim 2 of the '017 patent teaches using amplified DNA II in the transformed CHO cells of the invention. Therefore, the combined teachings of claim 12 of the '665 patent and claim 2 of the '017 patent render claim 5 of the '275 patent obvious.[3] As such, claim 5 of the '275 patent is virtually identical to or not patentably distinct from either claim 12 of the '665 patent itself or claim 12 of the '665 patent in light of claim 2 of the '017 patent.

Claim 6 of the '275 patent is invalid for double patenting in light of claim 12 of the '665 and claim 2 of the '017 patent (both set forth above with respect to claim 5) and claim 11 of the '665 patent, which reads:

> '665, cl. 11. A process in accordance with claim 10, wherein the gene associated with drug resistance is the gene coding for a mutant dihydrofolate reductase which renders cells resistant to methotrexate. → 10. A process in accordance with claim 1, wherein said DNA II which codes for a selectable phenotype comprises a gene associated with drug resistance. → 1. A process for inserting foreign DNA I into a suitable eucaryotic cell which comprises cotransforming said eucaryotic cell with said foreign DNA I and with unlinked foreign DNA II which codes for a selectable phenotype not expressed by said eucaryotic cell, said cotransformation being carried out under suitable conditions permitting survival or identification of eucaryotic cells which have

[3] The motivation to combine these claims is that they are contained in related applications and that they are directed to the same technology. This is the same motivation to combine that applies to all of the other combinations discussed throughout this request for reexamination. For the sake of efficiency, an explicit discussion of the motivation to combine claims from the Prior Axel Patents to render the claims of the '275 patent obvious will not be repeated.

> acquired said selectable phenotype, said foreign DNA II being attached to bacterial plasmid or phage DNA.

Claim 6 of the '275 patent depends from claim 5 of the '275 patent and adds only a limitation that the "DNA II encodes a dihydrofolate reductase which renders the transformed CHO cell resistant to methotrexate." This is expressly taught by claim 11 of the '665 patent. Although claim 11 of the '665 patent is not a product claim like claim 6 of the '275 patent, it nevertheless discloses a product virtually identical to or not patentably distinct from the product of claim 6 of the '275 patent. Regardless, claim 12 of the '665 patent and claim 2 of the '017 patent are product claims. Therefore, claim 6 of the '275 patent is virtually identical to or not patentably distinct from claim 11 of the '665 patent itself, or claim 12 of the '665 patent in light of claim 2 of the '017 patent and claim 11 of the '665 patent.

Claims 7, 8, and 9

> Claims 7, 8, and 9 of the '275 patent read as follows:
>
> 7. The transformed Chinese Hamster Ovary cell of claim 5, wherein the DNA I is attached to bacterial plasmid DNA.
>
> 8. The transformed Chinese Hamster Ovary cell of claim 5, wherein the DNA II is attached to bacterial plasmid DNA.
>
> 9. The transformed Chinese Hamster Ovary cell of claim 5, wherein both DNA I and DNA II is attached to bacterial plasmid DNA.

Claims 7, 8, and 9 of the '275 patent are invalid for double patenting in light of claim 12 of the '665 patent and claim 2 of the '017 patent (both set forth above with respect to claim 5 of the '275 patent) and claim 3 of the '665 patent, which reads:

> '665, cl. 3. A process in accordance with claim 1, wherein the DNA I or DNA II is attached to bacterial plasmid DNA. → 1. A process for inserting foreign DNA I into a suitable eucaryotic cell which comprises cotransforming said eucaryotic cell with said foreign DNA I and with unlinked foreign DNA II which codes for a selectable phenotype not expressed by said eucaryotic cell, said

> cotransformation being carried out under suitable conditions permitting survival or identification of eucaryotic cells which have acquired said selectable phenotype, said foreign DNA II being attached to bacterial plasmid or phage DNA.

Each of claims 7, 8, and 9 of the '275 patent depend from claim 5 of the '275 patent and add a single limitation, that the DNA I, DNA II, or both are attached to bacterial plasmid DNA. Each of these additional limitations is expressly claimed by claim 3 of the '665 patent, which claims either "DNA I or DNA II is attached to bacterial plasmid DNA." And, since claim 3 of the '665 patent both (a) recites DNA I can be attached to bacterial plasmid DNA and (b) is dependent upon claim 1 of the '665 patent, which states DNA II can be attached to bacterial plasmid DNA, it expressly claims "both DNA I and DNA II ... attached to bacterial plasmid DNA", as claimed in claim 9 of the '275 patent.

Although claim 3 of the '665 patent is not a product claim like claims 7, 8, and 9 of the '275 patent, it nevertheless discloses a product not patentably distinct from the product of claims 7, 8, and 9 of the '275 patent. Regardless, claim 12 of the '665 patent and claim 2 of the '017 patent are product claims like claims 7, 8, and 9 of the '275 patent. Therefore, claims 7, 8, and 9 of the '275 patent are virtually identical to or not patentably distinct from either claim 3 of the '665 patent itself or claim 12 of the '665 patent in light of claim 2 of the '017 patent and claim 3 of the '665 patent.

Claims 10, 11, and 12

Claims 10, 11, and 12 of the '275 patent read as follows:

> 10. The transformed Chinese Hamster Ovary cell of claim 5, wherein the DNA I is attached to phage DNA.
>
> 11. The transformed Chinese Hamster Ovary cell of claim 5, wherein the DNA II is attached to phage DNA.
>
> 12. The transformed Chinese Hamster Ovary cell of claim 5, wherein both DNA I and DNA II is attached to phage DNA.

Claims 10, 11, and 12 of the '275 patent are invalid for double patenting in light of claim 12 of the '665 patent and claim 2 of the '017 patent (both set forth above with respect to claim 5) and claim 2 of the '665 patent, which reads:

> '665, cl. 2. A process in accordance with claim 1, wherein the DNA I or KNA II is attached to phage DNA and encapsidated in a phage particle. → 1. A process for inserting foreign DNA I into a suitable eucaryotic cell which comprises cotransforming said eucaryotic cell with said foreign DNA I and with unlinked foreign DNA II which codes for a selectable phenotype not expressed by said eucaryotic cell, said cotransformation being carried out under suitable conditions permitting survival or identification of eucaryotic cells which have acquired said selectable phenotype, said foreign DNA II being attached to bacterial plasmid or phage DNA.

Each of claims 10, 11, and 12 of the '275 patent depend from claim 5 of the '275 patent and add a single limitation, that the DNA I, DNA II, or both are attached to phage DNA. Each of these additional limitations is expressly claimed by claim 2 of the '665 patent, which claims either "DNA I or [D]NA II is attached to phage DNA" (the "KNA" in claim 2 of the '665 patent is an obvious misspelling). And, since claim 2 of the '665 patent both (a) recites DNA I can be attached to phage DNA and (b) is dependent upon claim 1 of the '665 patent, which states DNA II can be attached to phage DNA, it expressly recites "both DNA I and DNA II... attached to phage DNA", as claimed in claim 12 of the '275 patent.

Although claim 2 of the '665 patent is not a product claim like claims 10, 11, and 12 of the '275 patent, it nevertheless discloses a product not patentably distinct from the product of claims 10, 11, and 12 of the '275 patent. Regardless, claim 12 of the '665 patent and claim 2 of the '017 patent are product claims like claims 10, 11, and 12 of the '275 patent. Therefore, claims 10, 11, and 12 of the '275 patent are virtually identical to or not patentably distinct from either claim 2 of the '665 patent itself or claim 12 of the '665 patent in light of claim 2 of the '017 patent and claim 2 of the '665 patent.

Claims 13, 14, and 15

Claims 13, 14, and 15 of the '275 patent read as follows:

> 13. The transformed Chinese Hamster Ovary cell of any of claims 5-12, further comprising the proteinaceous material.
>
> 14. A method of producing a proteinaceous protein which comprises culturing transformed CHO cells of claim 5 under suitable conditions to produce the proteinaceous material and recovering the proteinaceous material so produced.
>
> 15. The method of claim 14, wherein the proteinaceous material is glycoprotein.

Claims 13 of the '275 patent is invalid for double patenting in light of claim 12 of the '665 patent and claim 2 of the '017 patent (both set forth above with respect to claim 5) and claim 5 of the '017 patent, which reads:

> '017, cl. 5. A method of obtaining a proteinaceous protein which comprises culturing transformed cells in accordance with claim 1 under suitable conditions and recovering the proteinaceous material from the transformed cells so cultured. → 1. A transformed Chinese Hamster Ovary cell which comprises amplified foreign DNA I corresponding to a gene of interest stably incorporated into the chromosomal DNA of the transformed cell and amplified DNA II encoding a dominant selectable phenotype not expressed by the transformed cell prior to transformation.

Claim 13 of the '275 patent depends from any of claims 5 - 12 of the '275 patent and adds a single limitation that the CHO cell has some of the proteinaceous material. This additional limitation is expressly disclosed by or inherent in the claims of the Prior Axel Patents. For example, claim 5 of the '017 patent expressly teaches protein being recovered from the CHO cells, meaning that the CHO cells must have some of the proteinaceous material inside them, else it would not be possible to recover any.

During prosecution, Axel et al. argued that claim 13 of the '275 patent was unobvious over the Prior Axel Patents because it recites "glycoprotein." Amendment, February

12, 2002. However, no such recitation actually appears in claim 13 of the '275 patent. Therefore, claim 13 of the '275 patent is virtually identical to or not patentably distinct from claim 12 of the '665 patent in light of claims 2 and 5 of the '017 patent.

Claims 14 and 15 of the '275 patent are invalid for double patenting in light of claim 12 of the '665 patent and claim 2 of the '017 patent (both set forth above with respect to claim 5) and claim 14 of the '665 patent, which reads:

> '665, cl. 14. A process for producing a proteinaceous material which comprises cotransforming a suitable eucaryotic cell in accordance with the process of claim 1, maintaining the cotransformed eucaryotic cell under suitable conditions permitting production of the proteinaceous material and recovering the proteinaceous material so produced. → 1. A process for inserting foreign DNA I into a suitable eucaryotic cell which comprises cotransforming said eucaryotic cell with said foreign DNA I and with unlinked foreign DNA II which codes for a selectable phenotype not expressed by said eucaryotic cell, said cotransformation being carried out under suitable conditions permitting survival or identification of eucaryotic cells which have acquired said selectable phenotype, said foreign DNA II being attached to bacterial plasmid or phage DNA.

Claim 14 of the '275 patent is a method claim that "cultures" the CHO cell of claim 5 of the '275 patent "under suitable conditions to produce the proteinaceous material" and then "recover[s] the proteinaceous material so produced." These additional elements are expressly claimed by claim 14 of the '665 patent. Therefore, claim 14 of the '275 patent is virtually identical to or not patentably distinct from claim 12 of the '665 patent in light of claim 2 of the '017 patent and claim 14 of the '665 patent.

Claim 15 of the '275 patent depends from claim 14 of the '275 patent and adds a single limitation, that "the proteinaceous material is glycoprotein." Glycoprotein is discussed throughout the specification of each of the Prior Axel Patents as being an example, if not a targeted, proteinaceous material appropriate for the Axel et al. invention. See, e.g., '216 patent,

col. 3, lines 14-18 ("[i]t is therefore another important object of this invention to provide a process for producing compounds which include ... proteinaceous moieties such as glycoproteins"); '216 patent, col. 6, lines 39-43 ("the invention provides a process for producing partially proteinaceous products such as the glycoproteins"). Therefore, the claims of the Prior Axel Patents directed to a CHO cell encoding a proteinaceous material, such as claim 2 of the '017 patent, inherently claim or render obvious a CHO cell encoding a glycoprotein as claimed in claim 15 of the '275 patent. Therefore, claim 15 of the '275 patent is virtually identical to or not patentably distinct from claim 12 of the '665 patent in light of claim 2 of the '017 patent and claim 14 of the '665 patent.

Claim 16

Claim 16 of the '275 patent reads as follows:

> 16. A transformed Chinese Hamster Ovary (CHO) cell which comprises amplified foreign DNA I corresponding to a gene encoding a glycoprotein of interest and amplified DNA II encoding a dominant selectable phenotype not expressed by the transformed CHO cell prior to transformation, and both DNA I and DNA II being stably incorporated into the chromosomal DNA of the transformed Chinese Hamster Ovary cell.

Claim 16 of the '275 patent is invalid for double patenting in light of claim 2 of the '017 patent (set forth above with respect to claim 5). The only difference between claim 16 of the '275 patent and claim 2 of the '017 patent is that claim 16 of the '275 patent recites "DNA I corresponding to a gene encoding a glycoprotein of interest" while claim 2 of the '017 patent recites "DNA I encodes a proteinaceous material." Glycoprotein is discussed throughout the specification of each of the Prior Axel Patents as being an example, if not a targeted, proteinaceous material appropriate for the Axel et al. invention. See, e.g., '216 patent, col. 3, lines 14-18 ("[i]t is therefore another important object of this invention to provide a process for producing compounds which include ... proteinaceous moieties such as glycoproteins"); '216

patent, col. 6, lines 39-43 ("the invention provides a process for producing partially proteinaceous products such as the glycoproteins"). Therefore, the claims of the Prior Axel Patents directed to a CHO cell encoding a proteinaceous material, such as claim 2 of the '017 patent, inherently claim or render obvious a CHO cell encoding a glycoprotein as claimed in claim 16 of the '275 patent. Therefore, claim 16 of the '275 patent is virtually identical to or not patentably distinct from claim 2 of the '017 patent.

Claims 17, 18, and 19

Claims 17, 18, and 19 of the '275 patent read as follows:

> 17. The transformed Chinese Hamster Ovary cell of claim 16, wherein DNA II encodes a dihydrofolate reductase which renders the transformed cell resistant to methotrexate.
>
> 18. The transformed Chinese Hamster Ovary cell of claim 16, wherein DNA I or DNA II or both DNA I and DNA II is attached to bacterial plasmid DNA or phage DNA.
>
> 19. The transformed Chinese Hamster Ovary cell of any of claims 16-18, further comprising the glycoprotein of interest.

Claim 17 of the '275 patent is invalid for double patenting in light of claim 2 of the '017 patent (set forth above with respect to claim 5) and claim 4 of the '017 patent, which reads:

> '017, cl. 4. The transferred Chinese Hamster Ovary cell of claim 1, wherein DNA II encodes a dihydrofolate reductase which renders the transformed cell resistant to methotrexate. → 1. A transformed Chinese Hamster Ovary cell which comprises amplified foreign DNA I corresponding to a gene of interest stably incorporated into the chromosomal DNA of the transformed cell and amplified DNA II encoding a dominant selectable phenotype not expressed by the transformed cell prior to transformation.

Claim 17 of the '275 patent depends from claim 16 of the '275 patent and adds only a limitation that the "DNA II encodes a dihydrofolate reductase which renders the transformed CHO cell resistant to methotrexate." This additional limitation is expressly claimed by claim 4 of the '017

patent. Therefore, claim 17 of the '275 patent is virtually identical to or not patentably distinct from claim 2 of the '017 patent in light of claim 4 of the '017 patent.

Claim 18 of the '275 patent is invalid for double patenting in light of claim 12 of the '665 patent and claim 2 of the '017 patent (both set forth above with respect to claim 5). Claim 18 of the '275 patent depends from claim 16 of the '275 patent and adds only a limitation that the "DNA I or DNA II or both DNA I and DNA II is attached to bacterial plasmid DNA or phage DNA." This additional limitation is expressly taught by claim 12 of the '665 patent. Therefore, claim 18 of the '275 patent is virtually identical to or not patentably distinct from claim 2 of the '017 patent in light of claim 12 of the '665 patent.

Claim 19 of the '275 patent is invalid for double patenting in light of claim 2 of the '017 patent (set forth above with respect to claim 5) and claim 5 of the '017 patent, which reads:

> '017, cl. 5. A method of obtaining a proteinaceous protein which comprises culturing transformed cells in accordance with claim 1 under suitable conditions and recovering the proteinaceous material from the transformed cells so cultured. → 1. A transformed Chinese Hamster Ovary cell which comprises amplified foreign DNA I corresponding to a gene of interest stably incorporated into the chromosomal DNA of the transformed cell and amplified DNA II encoding a dominant selectable phenotype not expressed by the transformed cell prior to transformation.

Claim 19 of the '275 patent depends from any of claims 16 - 18 of the '275 patent and adds a single limitation that the CHO cell has some of the "glycoprotein of interest." This additional limitation is expressly disclosed by or inherent in the claims of the Prior Axel Patents. For example, claim 5 of the '017 patent expressly teaches protein being recovered from the CHO cells, meaning that the CHO cells must have some of the proteinaceous material inside them, else it would not be possible to recover any.

Further, Glycoprotein is discussed throughout the specification of each of the Prior Axel Patents as being an example, if not a targeted, proteinaceous material appropriate for the Axel et al. invention. See, e.g., '216 patent, col. 3, lines 14 – 18 ("[i]t is therefore another important object of this invention to provide a process for producing compounds which include ... proteinaceous moieties such as glycoproteins"); '216 patent, col. 6, lines 39 – 43 ("the invention provides a process for producing partially proteinaceous products such as the glycoproteins"). Therefore, the claims of the Prior Axel Patents directed to a CHO cell encoding a proteinaceous material, such as claims 2 and 5 of the '017 patent, inherently claim or render obvious a CHO cell encoding a glycoprotein as claimed in claim 19 of the '275 patent. As such, claim 19 of the '275 patent is virtually identical to or not patentably distinct from claim 2 of the '017 patent in light of claim 5 of the '017 patent.

Claim 20

Claim 20 of the '275 patent reads as follows:

> 20. A DNA construct for expression in Chinese Hamster Ovary (CHO) cells comprising DNA I encoding a proteinaceous material foreign to such CHO cells and linked thereto DNA II encoding a dihydrofolate reductase which is not expressed by such CHO cells and renders such CHO cells resistant to methotrexate when the CHO cells are transformed with the construct, the construct being effective for producing the proteinaceous material when the construct is introduced into such CHO cells.

Claim 20 of the '275 patent is invalid for double patenting in light of and claims 2 and 4 of the '017 patent and claim 70 of the '216 patent, which read:

> '017, cl. 2. The transferred Chinese Hamster Ovary cell of claim 1, wherein foreign DNA I encodes a proteinaceous material which is not associated with a selectable phenotype. → 1. A transformed Chinese Hamster Ovary cell which comprises amplified foreign DNA I corresponding to a gene of interest stably incorporated into the chromosomal DNA of the transformed cell and amplified DNA II encoding a dominant selectable phenotype not expressed by the transformed cell prior to transformation.

'017, cl. 4. The transferred Chinese Hamster Ovary cell of claim 1, wherein DNA II encodes a dihydrofolate reductase which renders the transformed cell resistant to methotrexate. → 1. A transformed Chinese Hamster Ovary cell which comprises amplified foreign DNA I corresponding to a gene of interest stably incorporated into the chromosomal DNA of the transformed cell and amplified DNA II encoding a dominant selectable phenotype not expressed by the transformed cell prior to transformation.

'216, cl. 70. A process in accordance with claim 69 wherein said gene associated with resistance to a drug or chemical anatgonist is a gene coding for a mutant dihydrofolate reductase which renders cells resistant to methotrexate. → 69. A process in accordance with claim 54 wherein said DNA II which codes for proteinaceous material which is associated with a selectable phenotype comprises a gene associated with resistance to a drug or chemical antagonist. → 54. A process for generating a multiplicity of foregin DNA I molecules corresponding to multiple copies of a gene in a eucaryotic cell which comprises tranforming said eucaryotic cell with a molecule which is formed by linking one of said foreign DNA I molecules to a DNA II molecule corresponding to an amplifiable gene for a dominant selectable phenotype not expressed by said eucaryotic cell, and culturing the transformed eucaryotic cells in the presence of successively elevated concentrations of an agent permitting survival or identification of eucaryotic cells which have acquired multiple copies of said amplifiable gene, said transformation and culturing being carried out under suitable conditions.

The only difference between claim 20 of the '275 patent and claim 2 of the '017 patent is that claim 20 of the '275 patent contains the limitation "DNA II encoding a dihydrofolate reductase." This limitation is expressly claimed in claim 4 of the '017 patent. Therefore, claim 20 of the '275 patent is virtually identical to or not patentably distinct from claim 2 of the '017 patent in light of claim 4 of the '017 patent.

During prosecution of the '275 patent, Axel et al. argued that none of the claims of the Prior Axel Patents make obvious the "linked" limitation contained in claim 20 of the '275 patent. Amendment, February 12, 2002. However, claims 2 and 4 of the '017 patent depend

from claim 1 of the '017 patent, which is not limited to either linked or unlinked DNA II. Therefore, they claim both.

Further, claim 70 of the '216 patent expressly contains both the "dihydrofolate reductase" and the "linked" limitations. Although claim 70 of the '216 patent is not a product claim like claim 20 of the '275 patent, claim 70 of the '216 patent discloses a "molecule which is formed" that is nothing more than the "DNA construct" of claim 20 of the '275 patent. Therefore, claim 20 of the '275 patent is also virtually identical to or not patentably distinct from claim 70 of the '216 patent.

CONCLUSION

For the reasons set forth above, each claim of the '275 patent is invalid for double patenting in light of the Prior Axel Patents. PUBPAT respectfully requests that they be reexamined ex parte.

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