Chapter 2400 Biotechnology

2401 Introduction [R–3]

This chapter provides guidance on the practices and procedures for implementation of the deposit rules (37 CFR 1.801 – 1.809) and the sequence rules (37 CFR 1.821 – 1.825). The final rule for deposits of biological materials for patent purposes was published in the *Federal Register*, 54 Fed. Reg. 34864 (August 22, 1989) and in

the *Official Gazette*, 1106 O.G. 37 (September 12, 1989). The deposit rules went into effect on January 1, 1990. The final rule for the requirements for patent applications containing nucleotide sequence and/or amino acid sequence disclosures was published in the *Federal Register*, 55 Fed. Reg. 18230 (May 1, 1990) and in the *Official Gazette*, 1114 O.G. 29 (May 15, 1990). The sequence rules went into effect on October 1, 1990.

Additional information regarding the development of the deposit rules can be obtained in the text of the draft policy statement, published in BNA's *Patent, Trademark and Copyright Journal*, 32 PTCJ 781 at 76, 90 (May 22, 1986), the advanced notice of proposed rulemaking, published in the *Federal Register*, 52 Fed. Reg. 34080 (September 9, 1987), and in the *Official Gazette*, 1082 O.G. 47 (September 29, 1987) and in the notice of proposed rulemaking, published in the *Federal Register*, 53 Fed. Reg. 39420 (October 6, 1988), and in the *Official Gazette*, 1095 O.G. 47 (October 25, 1988). Additional information regarding the development of the sequence rules can be obtained in the text of the notice of proposed rulemaking, published in the *Federal Register*, 54 Fed. Reg. 18671 (May 2, 1989) and in the *Official Gazette*, 1102 O.G. 34 (May 16, 1989).

>See MPEP § 803.04 and § 1850 for restriction and unity of invention practice respectively in patent applications claiming independent and distinct nucleotide sequences.<

2402 The Deposit Rules [R-3]

Every patent must contain a written description of the invention sufficient to enable a person skilled in the art to which the invention pertains to make and use the invention. Where the invention involves a biological material and words alone cannot sufficiently describe how to make and use the invention in a reproducible manner, access to the biological material may be necessary for the satisfaction of the statutory requirements for patentability under 35 U.S.C. 112. Courts have recognized the necessity and desirability of permitting an applicant for a patent to supplement the written disclosure in an application with a deposit of biological material which is essential to meet some requirement of the statute with respect to the claimed invention. *Merck and Co., Inc.* v. *Chase Chemical Co.*, 273 F. Supp. 68, 155 USPQ 139 (D. N.J. 1967); *In re Argoudelis*, 434 F.2d 666, 168 USPQ 99 (CCPA 1970). To facilitate the recognition of deposited biological material in patent applications throughout the world, the Budapest Treaty on the International Recognition of the Deposit of Micro-organisms for the Purposes of Patent Procedure was established in 1977, and became operational in 1981. The Treaty requires signatory countries, like the United States, to recognize a deposit with any depository which has been approved by the World Intellectual Property Organization (WIPO).

The deposit rules (37 CFR 1.801 – 1.809) set forth examining procedures and conditions of deposit which must be satisfied in the event a deposit is required. The rules do not address the substantive issue of whether a deposit is required under any particular set of facts.

The rules are effective for all applications filed on or after January 1, 1990, and for all reexamination proceedings in which the request for reexamination was filed on or after January 1, 1990, except that deposits made prior to the effective date which were acceptable under the then current practice will be acceptable in such applications and proceedings. Since most of the provisions of the rules reflect policy and practice existing prior to January 1, 1990, little change in practice or burden on applicants for patent and patent owners relying on the deposit of biological material has occurred. Applicants and patent owners are encouraged to comply with these rules even if their applications and reexamination proceedings were filed prior to January 1, 1990. **

2403 Deposit of Biological Material

37 CFR 1.801 Biological material.

For the purposes of these regulations pertaining to the deposit of biological material for purposes of patents for inventions under 35 U.S.C. 101, the term biological material shall include material that is capable of self-replication either directly or indirectly. Representative examples include bacteria, fungi including yeast, algae, protozoa, eukaryotic cells, cell lines, hybridomas, plasmids, viruses, plant tissue cells, lichens and seeds. Viruses, vectors, cell organelles and other non-living material existing in and reproducible from a living cell may be deposited by deposit of the host cell capable of reproducing the non-living material.

37 CFR 1.801 indicates that the rules pertaining to deposits for purposes of patents for inventions under 35 U.S.C. 101 are intended to relate to biological material. For the purposes of these rules, the term "biological material" is defined in terms of a non-exhaustive list of representative materials which can be deposited in accordance with the procedures defined in these rules. These rules are intended to address procedural matters in the deposit of biological material for patent purposes. They are not designed to decide substantive issues such as whether a deposit of a particular organism or material

would be recognized or necessary for the purposes of satisfying the statutory requirements for patentability under 35 U.S.C. 112. Although the issue of the need to make a deposit of biological material typically arises under the enablement requirement of the first paragraph of 35 U.S.C. 112, the issue could also arise under the description requirement (35 U.S.C. 112, first paragraph), best mode requirement (35 U.S.C. 112, first paragraph) or the requirements of the second paragraph of 35 U.S.C. 112 with respect to the claims.

37 CFR 1.801 does not attempt to identify what biological material either needs to be or may be deposited to comply with the requirements of 35 U.S.C. 112. For the most part, this issue must be addressed on a case-by-case basis. Thus, while the Office does not currently contemplate that there would be any situations where a material that is not capable of self-replication either directly or indirectly would be acceptable as a deposit, an applicant is clearly not precluded by these rules from attempting to show in any given application why the deposit of such a material should be acceptable to satisfy the requirements of 35 U.S.C. 112.

2403.01 Material Capable of Self-Replication

Biological material includes material that is capable of self-replication either directly or indirectly. Direct self-replication includes those situations where the biological material reproduces by itself. Representative examples of materials capable of self-replication are defined in the rule. Indirect self-replication is meant to include those situations where the biological material is only capable of replication when another self-replicating biological material is present. Self-replication after insertion in a host is one example of indirect self-replication. Examples of indirect replicating biological materials include viruses, phages, plasmids, symbionts, and replication defective cells. The list of representative examples of each type of replicating material includes viruses to demonstrate that the two lists in the rule are not intended to be mutually exclusive.

2403.02 Plant Material

Although plant material is included within the scope of the definition of biological material for purposes of patents for plant inventions under 35 U.S.C. 101, the rules on deposits are not applicable to applications filed under the Plant Patent Act (35 U.S.C. 161-164). The Office is of the view that a deposit is not required under the present provisions of 35 U.S.C. 162. Thus, a deposit is not necessary for the grant of a plant patent under the provisions of 35 U.S.C. 161-164. As with other biological material deposited for purposes of patents for inventions under 35 U.S.C. 101, the deposit of plant material together with the written specification must enable those skilled in the art to make and use the claimed invention, in accordance with the requirements of 35 U.S.C. 112.

As with some types of reproducible biological material, seeds can be reproduced only after a growing season which may be relatively long. Although the rules do not specify a specific number of seeds to be deposited to meet the requirements of these rules, the Office will consider 2500 to be a minimum number in the normal case, but will give an applicant the opportunity to provide justification why a lesser number would be suitable under the circumstances of a particular case. The Department of Agriculture requires a deposit of 2500 seeds for the grant of a Plant Variety Protection Certificate under the Plant Variety Protection Act (7 U.S.C. 2321 *et seq.*). As the reproduction of seeds will often take a substantial period of time, the Office will require, at a minimum for the grant of a patent, a number of seeds that is likely to satisfy demand for samples once the patent is granted. In one instance, the Office accepted a deposit of 600 seeds coupled with an undertaking to deposit 1900 more seeds with due diligence. The particular situation involved a "seedless" vegetable with very few seeds per "fruit;" about two growing seasons were required to provide the additional 1900 seeds.

2404 Need or Opportunity to Make a Deposit

37 CFR 1.802 Need or Opportunity to make a deposit.

(a) Where an invention is, or relies on, a biological material, the disclosure may include reference to a deposit of such biological material.

(b) Biological material need not be deposited unless access to such material is necessary for the satisfaction of the statutory requirements for patentability under 35 U.S.C. 112. If a deposit is necessary, it shall be acceptable if made in accordance with these regulations. Biological material need not be deposited, inter alia, if it is known and readily available to the public or can be made or isolated without undue experimentation. Once deposited in a depository complying with these regulations, a biological material will be considered to be readily available even though some requirement of law or regulation of the United States or of the country in which the depository institution is located permits access to the material only under conditions imposed for safety, public health or similar reasons.

(c) The reference to a biological material in a specification disclosure or the actual deposit of such material by an applicant or patent owner does not create any presumption that such material is necessary to satisfy 35 U.S.C. 112 or that deposit in accordance with these regulations is or was required.

37 CFR 1.802(a) permits a deposit of a biological material to be referenced in a patent application where an invention is, or relies on, a biological material. The invention may rely on a biological material for the purposes of making or using the invention, either as a preferred mode or an alternative mode of operation. A reference to a deposit may be included in a specification even though the deposit is not required to satisfy the requirements of 35 U.S.C. 112.

There is no necessary implication or presumption that can or should be made about the need for a deposit simply because reference to a deposit is made in an application disclosure, as noted in paragraph (c). As noted in paragraph (b), biological material need not be deposited unless access to such material is necessary for the satisfaction of the statutory requirements for patentability under 35 U.S.C. 112 and that access is not otherwise available in the absence of a deposit. Where a deposit is required to provide the necessary access, a deposit is acceptable for patent purposes only where it is made in accordance with these regulations. Even where access to biological material is required to satisfy these statutory requirements, a deposit may not be necessary if access sufficient to satisfy these requirements is otherwise available.

2404.01 Biological Material That Is Known and Readily Available to the Public

In an application where the invention required access to specific biological material, an applicant could show that the biological material is accessible because it is known and readily available to the public. The concepts of "known and readily available" are considered to reflect a level of public accessibility to a necessary component of an invention disclosure that is consistent with an ability to make and use the invention. To avoid the need for a deposit on this basis, the biological material must be both known and readily available – neither concept alone is sufficient. A material may be known in the sense that its existence has been published, but is not available to those who wish to obtain that particular known biological material. Likewise, a biological material may be available in the sense that those having possession of it would make it available upon request, but no one has been informed of its existence.

The Board of Patent Appeals and Interferences has held that a description of the precise geographic location of marine tunicates, as a biological material, used in a claimed invention was adequate to satisfy the enablement requirement of 35 U.S.C. 112. *Ex Parte Rinehart*, 10 USPQ2d 1719 (Bd Pat. App. & Int. 1985). The term "readily" used in the phrase "known and readily available" is considered appropriate to define that degree of availability which would be reasonable under the circumstances. If the biological material and its natural location can be adequately described so that one skilled in the art could obtain it using ordinary skill in the art, the disclosure would appear to be sufficient to meet the enablement requirement of 35 U.S.C. 112 without a deposit so long as its degree of availability is reasonable under the circumstances.

By showing that a biological material is known and readily available or by making a deposit in accordance with these rules, applicant does not guarantee that such biological material will be available forever. Public access during the term of the patent may affect the enforceability of the patent. Although there is a public interest in the availability of a deposited biological material during and after the period of enforceability of the patent, there should not be any undue concern about continued access to the public. Unless there is a reasonable basis to believe that the biological material will cease to be available during the enforceable life of the patent, current availability would satisfy the requirement. The incentives provided by the patent system should not be constrained by the mere possibility that a disclosure that was once enabling would become non–enabling over a period of time through no fault of the patentee. *In re Metcalfe*, 410 F.2d 1378, 161 USPQ 789 (CCPA 1969).

If an applicant has adequately established that a biological material is known and readily available, the Office will accept that showing. In those instances, however, the applicant takes the risk that the material may cease to be known and readily available. Such a defect cannot be cured by reissue after the grant of a patent.

On the other hand, *Ex parte Humphreys*, 24 USPQ2d 1255 (Bd Pat. App. & Int. 1992), held that the only manner in which applicants could satisfy their burden of assuring public access to the needed biological material, and, thereby, compliance with the enablement requirement of 35 U.S.C. 112, was by making an appropriate

deposit. The fact that applicants and other members of the public were able to obtain the material in question from a given depository prior to and after the filing date of the application in issue did not establish that upon issuance of a patent on the application that such material would continue to be accessible to the public. The applicants did not make of record any of the facts and circumstances surrounding their access to the material in issue from the depository, nor was there any evidence as to the depository's policy regarding the material if a patent would have been granted. Further, there was no assurance that the depository would have allowed unlimited access to the material if the application had matured into a patent.

There are many factors that may be used as indicia that a biological material is known and readily available to the public. Relevant factors include commercial availability, references to the biological material in printed publications, declarations of accessibility by those working in the field, evidence of predictable isolation techniques, or an existing deposit made in accordance with these rules. Each factor may or may not be sufficient alone to demonstrate that the biological material is known and readily available. Those applicants that rely on evidence of accessibility other than a deposit take the risk that the patent may no longer be enforceable if the biological material necessary to satisfy the requirements of 35 U.S.C. 112 ceases to be accessible.

The Office will accept commercial availability as evidence that a biological material is known and readily available only when the evidence is clear and convincing that the public has access to the material. A product could be commercially available but only at a price that effectively eliminates accessibility to those desiring to obtain a sample. The relationship between the applicant relying on a biological material and the commercial supplier is one factor that would be considered in determining whether the biological material was known and readily available. However, the mere fact that the biological material is commercially available only through the patent holder or the patent holder's agents or assigns shall not, by itself, justify a finding that the necessary material is not readily available, absent reason to believe that access to the biological material would later be improperly restricted.

The mere reference to a deposit or the biological material itself in any document or publication does not necessarily mean that the deposited biological material is readily available. Even a deposit made under the Budapest Treaty and referenced in a United States or foreign patent document would not necessarily meet the test for known and readily available unless the deposit was made under conditions that are consistent with those specified in these rules, including the provision that requires, with one possible exception, that all restrictions on the accessibility be irrevocably removed by the applicant upon the granting of the patent. *Ex parte Hildebrand*, 15 USPQ2d 1662 (Bd Pat. App. & Int. 1990).

A Budapest Treaty deposit cited in a U.S. patent need not be made available if it was not required to satisfy 35 U.S.C. 112. Thus, a reference to a deposit will not be certified available unless either (1) the deposit was necessary to overcome a rejection under 35 U.S.C. 112, or (2) there is, in the record, a statement by the examiner that a rejection under 35 U.S.C. 112 would have been made "but for" the deposit (assumes deposit information in record, as filed). Otherwise, public access cannot be certified and the deposit cannot be relied upon for other purposes, e.g., the deposit cannot be relied upon by a third party to establish "known" and "readily available" in another application. See 37 CFR 1.808 and MPEP § 2410 and§ 2410.02.

Once a deposit is made in a depository complying with these rules, and under conditions complying with these rules, a biological material will be considered to be readily available even though some requirement of law or regulation in the United States or in the country where the depository institution is located permits access to the material only under conditions imposed for health, safety or similar reasons. This provision is consistent with the Budapest Treaty (Article 5) and is designed to permit the patenting of inventions involving materials having restricted distribution, where the restrictions are imposed for the public, as opposed to the private, welfare.

2404.02 Biological Material That Can Be Made or Isolated Without Undue Experimentation

Applicant may show that a deposit is not necessary even though specific biological materials are required to practice the invention if those biological materials can be made or isolated without undue experimentation. Deposits may be required to support the claims if an isolation procedure requires undue experimentation to

obtain the desired biological material. *Ex Parte Jackson*, 217 USPQ 804 (Bd App. 1982). No deposit is required, however,where the required biological materials can be obtained from publicly available material with only routine experimentation and a reliable screening test. *Tabuchi* v. *Nubel*, 559 F.2d 1183, 194 USPQ 521 (CCPA 1977); *Ex Parte Hata*, 6 USPQ 2d 1652 (Bd Pat. App. & Int. 1987).

2404.03 Reference to a Deposit in the Specification

37 CFR 1.802(c) specifically provides that the mere reference to a biological material in the specification disclosure or the actual deposit of such material does not create any presumption that such referenced or deposited material is necessary to satisfy 35 U.S.C. 112, or that a deposit in accordance with these regulations is or was required. It should be noted, however, that a reference to a biological material, present in an application upon filing, may form the basis for making a deposit, where required, after the filing date of a given application but that the reference to the biological material, itself, cannot be added after filing without risking the prohibited introduction of new matter (35 U.S.C. 132). See the discussion of the Lundak application in MPEP § 2406.01.

2405 Acceptable Depository [R–3]

37 CFR 1.803. Acceptable depository.

(a) A deposit shall be recognized for the purposes of these regulations if made in

(1) any International Depositary Authority (IDA) as established under the Budapest Treaty on the International Recognition of the Deposit of Micro–organisms for the Purposes of Patent Procedure, or

(2) any other depository recognized to be suitable by the Office. Suitability will be determined by the Commissioner on the basis of the administrative and technical competence, and agreement of the depository to comply with the terms and conditions applicable to deposits for patent purposes. The Commissioner may seek the advice of impartial consultants on the suitability of a depository. The depository must:

(i) Have a continuous existence;

(ii) Exist independent of the control of the depositor;

(iii) Possess the staff and facilities sufficient to examine the viability of a deposit and store the deposit in a manner which ensures that it is kept viable and uncontaminated;

(iv) Provide for sufficient safety measures to minimize the risk of losing biological material deposited with it;

(v) Be impartial and objective;

(vi) Furnish samples of the deposited material in an expeditious and proper manner; and

(vii) Promptly notify depositors of its inability to furnish samples, and the reasons why.

(b) A depository seeking status under paragraph (a)(2) of this section must direct a communication to the Commissioner which shall:

(1) Indicate the name and address of the depository to which the communication relates;

(2) Contain detailed information as to the capacity of the depository to comply with the requirements of paragraph (a) (2) of this section, including information on its legal status, scientific standing, staff and facilities;

(3) Indicate that the depository intends to be available, for the purposes of deposit, to any depositor under these same conditions;

(4) Where the depository intends to accept for deposit only certain kinds of biological material, specify such kinds;

(5) Indicate the amount of any fees that the depository will, upon acquiring the status of suitable depository under paragraph (a) (2) of this section, charge for storage, viability statements and furnishings of samples of the deposit.

(c) A depository having status under paragraph (a)(2) of this section limited to certain kinds of biological material may extend such status to additional kinds of biological material by directing a communication to the Commissioner in accordance with paragraph (b) of this section. If a previous communication under paragraph (b) of this section is of record, items in common with the previous communication may be incorporated by reference.

(d) Once a depository is recognized to be suitable by the Commissioner or has defaulted or discontinued its performance under this section, notice thereof will be published in the Official Gazette of the Patent and Trademark Office.

37 CFR 1.803 indicates that a depository will be recognized as acceptable for the purposes of these regulations if it is either an International Depository Authority (IDA) established under the Budapest Treaty, or if it is a depository recognized as suitable by the Commissioner. After the effective date of these regulations, a deposit of biological material which is made in a depository which is not recognized as acceptable under this regulation will not be considered as satisfying the requirements of 35 U.S.C. 112. See *Ex parte Humphreys*, 24 USPQ2d 1255 (Bd Pat. App. & Int. 1992). On the other hand, if a deposit is not required to satisfy the requirements of 35 U.S.C. 112, it is permissible to make reference to such a deposit even though it may not be in a depository or made under the conditions which are acceptable under these regulations. As new depositories are accepted under the Budapest Treaty or are recognized as suitable by the Commissioner, their identity will be announced in the *Official Gazette*.

An organization may be recognized as suitable by the Office if the procedure and conditions specified in 37 CFR 1.803(a)(2) and 37 CFR 1.803(b) are followed. Generally, it is not the intention of the Office to recognize as suitable any organization where the need for a suitable depository for patent purposes is being met by depositories recognized as IDAs under the Budapest

Treaty. Suitability will be judged by the Commissioner, based on need and the information supplied by the organization seeking status, and information obtained from other sources that may be consulted.

While there is a desire to provide flexibility to a patent applicant in selecting an appropriate depository, these rules are not intended to permit each patent applicant to become its own depository since both the patent owner and the public have an interest in the continued availability and accessibility of the deposit during the enforceable life of the patent, and the public has a continuing interest in its availability when the patent is no longer enforceable. The concept of a depository independent of the control of the depositor or an IDA as an acceptable depository is based on the need and desire to ensure the safe and reliable storage of a deposited biological material under circumstances that are substantially free of the opportunity for intentional mishandling or negligent handling of the deposited material. The use of an independent depository or internationally recognized depository will tend to preserve the integrity of the deposit process against those that may accidentally alter the deposited material, may wish to tamper with the deposited material or may wish to resume control of its availability when the patent is no longer enforceable, and will tend to preserve the interest of the public in the access to the biological material once the term of the patent expires.

When a depository having status under 37 CFR 1.803(a)(2) seeks to change the kinds of biological materials that it will accept and maintain for the purposes of these rules, a communication requesting such a change should be directed to the Commissioner containing the information requested in 37 CFR 1.803(b). When such a change is requested, the requesting depository should provide a complete list of the kinds of biological materials it will accept.

37 CFR 1.803(d) indicates that once a depository is recognized as suitable for the purposes of this rule, or has defaulted or discontinued its performance under this section, notice thereof will be published in the *Official Gazette* of the Patent and Trademark Office. A current list (as of January, *>1997<) of IDAs recognized under the Budapest Treaty, with addresses, is included below. The mere fact that a deposit has been made in one of these depositories does not mean that the terms of the deposit meet either the requirements of the Budapest Treaty or the deposit regulations. Many of the depositories recognized under the Budapest Treaty have many different arrangements under which biological material may be stored.

The World Intellectual Property Organization (WIPO) publishes a Guide to the Deposit of Micro-organisms under the Budapest Treaty (WIPO Publication No. 661 (E)) on the procedures and requirements concerning the deposit of biological material, including procedures for obtaining a sample of deposited material, in each of the international depositary authorities.

CURRENT IDAs

The following constitutes the list of IDAs recognized under the Budapest Treaty. The list is current as of January, *>1997<.

>Advanced Biotechnology Center (ABC)
Interlab Cell Line Collection
(Biotechnology Dept)
Largo Rossana Benzi, 10
16132 Genova
Italy<

Agricultural Research Service Culture Collection (NRRL)
1815 North University Street
Peoria, Illinois 61604
USA

**

All-Union Scientific Center of Antibiotics (VNIIA)
Nagatinskaya Street 3-a
113105 Moscow
Russian Federation

American Type Culture Collection (ATCC)
12301 Parklawn Drive
Rockville, Maryland 20852
USA

Australian Government Analytical Laboratories (AGAL)
The New South Wales Regional Laboratory
1, Suakin Street
Pymble, NSW 2073
Australia

Belgian Coordinated Collections of Microorganisms (BCCM)
Prime Minister's Services
**>Federal Office for Scientific, Technical and Cultural Affairs (OSTC)<

Rue de la Science 8
B–*>1000< Brussells
Belgium

Centraalbureau Voor Schimmelcultures (CBS)
Oosterstraat 1
Postbus 273
NL–3740 AG Baarn
Netherlands

>China Center for Type Culture Collection (CCTCC)
Wuhan University
Wuhan 430072
China

China General Microbiological Culture Collection Center (CGMCC)
China Committee for Culture Collection of Microorganisms
P.O. Box 2714
Beijing 100080
China<

Colleción Española de Cultivos Tipo (CECT)
Microbiology Department
Biological Science Faculty
46100 Burjasot (Valencia)
Spain

Collection Nationale De *>Cultures< De Micro–organismes (CNCM)
Institut Pasteur
28, rue du Dr Roux
75724 Paris Cédex 15
France

Culture Collection of Algae and Protozoa (CCAP)
Institute of Freshwater Ecology
Windermere Laboratory
Ambleside, Cumbria LA22 0LP
United Kingdom
and Dunstaffnage Marine Laboratory
P.O. Box 3
Oban, Argyll PA34 4AD
United Kingdom

>Culture Collection of Yeasts (CCY)
Institute of Chemistry
Slovak Academy of Sciences
Dúbravská cesta 9
842 38 Bratislava,
Slovakia<

Czech Collection of Microorganisms (CCM)
Ceskoslovenská sbírka mikroorganismu
*>Masary< University
ul. Tvrdého c. 14
602 00 Brno
Czech Republic

**

>DSMZ–< Deutsche Sammlung Von Mikroorganismen und ZellKulturen GmbH (>DSMZ<)
Mascheroder Weg 1b
D–*>38124< Braunschweig
Germany

European Collection of Animal Cell Cultures (ECACC)
Vaccine Research and Production Laboratory
Public Health Laboratory Service
Centre for Applied Microbiology and Research
Porton Down
Salisbury, Wiltshire SP4 0JG
United Kingdom

**

International Mycological Institute (IMI)
Bakeham Lane
Englefield Green
Egham, Surrey TW20 9TY
United Kingdom

>Korean Cell Line Research Foundation (KCLRF)
Cancer Research Institute
Seoul National University College of Medicine
28 Yungon–dong, Chongno–gu
Seoul 110–799
Republic of Korea<

Korea **>Research Institute of Bioscience and Biotechnology (KRIBB)<
*>52<, Oun–Dong
Yusong–*>Ku<
Taejon >305–333<
Republic of Korea

Korean Culture Center of Microorganisms (KCCM)
College of Engineering
Yonsei University
Sodaemun gu
Seoul 120–749
Republic of Korea

National Bank for Industrial Microorganisms and Cell Cultures (NBIMCC)
125, **>Tsarigradskochausse Blvd.<
Block 2
>1113< Sofia
Bulgaria

National Collection of Agricultural and Industrial Microorganisms (NCAIM)
Department of Microbiology and Biotechnology
University of Horticulture and the Food Industry
Somlói út 14–16
H–1118 Budapest
Hungary

National Collection of Food Bacteria (NCFB)
AFRC Institute of Food Research
Reading Laboratory
*>Earley Gate, Whiteknights Road<
Reading *>, Berkshire RG6 2EF<
United Kingdom

National Collection of Type Cultures (NCTC)
Central Public Health Laboratory
61 Colindale Avenue
London, NW9 5HT
United Kingdom

National Collection of Yeast Cultures (NCYC)
AFRC Institute of Food Research
Norwich Laboratory
Colney Lane
Norwich NR4 7UA
United Kingdom

National Collections of Industrial and Marine Bacteria Limited (NCIMB)
23 St. Machar Drive
Aberdeen AB2 1RY
Scotland
United Kingdom

National Institute of Bioscience and Human–Technology (*>NIBH<)
**
Agency of Industrial Science and Technology
Ministry of International Trade and Industry
1–3, Higashi 1–chome
Tsukuba–shi
Ibaraki–ken 305
Japan

>Russian Collection of Microorganisms (VKM)
Prospekt Naouki, 5
142292 Pushchino (Moscow Region)
Russian Federation

Russian National Collection of Industrial Microorganisms (VKPM)
GNII Genetika
Dorozhny proezd. 1
Moscow 113545
Russian Federation<

2406 Time of Making an Original Deposit

37 CFR 1.804 Time of making an original deposit.

(a) Whenever a biological material is specifically identified in an application for patent as filed, an original deposit thereof may be made at any time before filing the application for patent or, subject to § 1.809, during pendency of the application for patent.

(b) When the original deposit is made after the effective filing date of an application for patent, the applicant shall promptly submit a verified statement from a person in a position to corroborate the fact, and shall state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which case the statement need not be verified.

37 CFR 1.804 specifies the time for making an original deposit to fulfill the requirements of 35 U.S.C. 112. For the reasons discussed throughout this section, it is recommended that a deposit be made before the filing date of the application. However, for the purposes of complying with the requirements of 35 U.S.C. 112, a deposit of a biological material may be made at any time before filing the application for patent or during the pendency of the application subject to the conditions of 37 CFR 1.809. Where a deposit is needed to satisfy the requirements of 35 U.S.C. 112 and it is made during the pendency of the application, it must be made no later than the time period set by the examiner at the time the Notice of Allowance and Issue Fee Due is mailed. A necessary deposit need not be made by an applicant until the application is in condition for allowance so long as the applicant provides a written assurance that an acceptable deposit will be made on or before the payment of the issue fee. This written assurance must provide sufficiently detailed information to convince the examiner that there is no outstanding issue regarding deposits that needs to be resolved.

These rules are equally applicable in the cases of international and national stage applications filed under

the Patent Cooperation Treaty. Insofar as the rules do not permit post-issuance original deposits, the failure to make an original deposit in an application cannot be cured by filing a reissue application or instituting a reexamination proceeding. However, if an amendment of claims in a reexamination proceeding raises the need for a deposit, an original deposit may be made during the reexamination proceeding.

2406.01 Description in Application Specification

37 CFR 1.804(a) specifies not only a permissible time frame for making an original deposit, but also specifies that the biological material deposited must be specifically identified in the application for patent as filed. The requirement for a specific identification is consistent with the description requirement of the first paragraph of 35 U.S.C. 112 and provides an antecedent basis for the biological material which either has been or will be deposited before the patent is granted.

The description in the Lundak application as filed (now patent 4,594,325) provides a suitable illustration of the specific identification and description which are required in an application as filed. In that application, an immortal B-cell line was disclosed and claimed. The cell line was referred to in the application, as filed, as WI-L2-729 HF2. The methods of obtaining and using this cell line were also described in the application as filed. A deposit of the cell line was made with the American Type Culture Collection (ATCC) about a week after the application was filed in the United States. The United States Court of Appeals for the Federal Circuit held that the requirements of access by the Office to a sample of the cell line during pendency, and public access after grant, were met by Lundak's procedures. The Court further held that the addition of information designating the depository, accession number, and deposit date of the deposited cell line in ATCC after the filing date did not violate the prohibition against new matter in 35 U.S.C. 132. *In re Lundak*, 773 F.2d 1216, 227 USPQ 90 (Fed. Cir. 1985). However, it must be clear from the application as filed that the invention claimed and described in the specification "was fully capable of being reduced to practice (i.e., no technological problems, the resolution of which would require more than ordinary skill and reasonable time, remained in order to obtain an operative, useful process)." *Feldman* v. *Aunstrup*, 517 F.2d 1351, 1355, 186 USPQ 108, 113 (CCPA 1975), *cert. denied*, 424 U.S. 912 (1976).

2406.02 Deposit After Filing Date – Corroboration

When the original deposit is made after the effective filing date of an application for patent, an applicant is required to promptly submit a verified statement from a person in a position to corroborate that the biological material which is deposited is a biological material specifically identified in the application (the filing date of which is relied upon) as filed. The nature of this corroboration will depend on the circumstances in the particular application under consideration, including the length of time between the application filing date and the date of deposit. While few, if any, situations can be imagined where the description requirement of 35 U.S.C. 112 can be satisfied where the biological material was not in existence at the time of filing, the rules will not preclude such a situation as there is no requirement in the patent law that an actual reduction to practice occur as a condition precedent to filing a patent application. The requirement for a verified statement is not necessary under 37 CFR 1.804(b) if the person making the statement is an attorney or agent registered to practice before the Office.

2406.03 Possible Loss of U.S. Filing Date in Other Countries

Those applicants intending to file patent applications in a country foreign to the United States relying upon biological material that must be deposited to satisfy the requirements of 35 U.S.C. 112 when the application is filed in the United States are cautioned that in many countries the deposit must be made before the filing date of the priority application in order to obtain foreign priority rights. Thus, while the deposit of a biological material subsequent to the effective filing date of a United States application is sufficient to comply with 35 U.S.C. 112, an applicant may not be able to rely on the filing date of such a U.S. application if a patent is sought in certain countries foreign to the United States.

2407 Replacement or Supplement of Deposit

37 CFR 1.805 Replacement or supplement of deposit.

(a) A depositor, after receiving notice during the pendency of an application for patent, application for reissue patent or reexamination proceeding, that the depository possessing a deposit either cannot

furnish samples thereof or can furnish samples thereof but the deposit has become contaminated or has lost its capability to function as described in the specification, shall notify the Office in writing, in each application for patent or patent affected. In such a case, or where the Office otherwise learns, during the pendency of an application for patent, application for reissue patent or reexamination proceeding, that the depository possessing a deposit either cannot furnish samples thereof or can furnish samples thereof but the deposit has become contaminated or has lost its capability to function as described in the specification, the need for making a replacement or supplemental deposit will be governed by the same considerations governing the need for making an original deposit under the provisions set forth in § 1.802(b). A replacement or supplemental deposit made during the pendency of an application for patent shall not be accepted unless it meets the requirements for making an original deposit under these regulations, including the requirement set forth under § 1.804(b). A replacement or supplemental deposit made in connection with a patent, whether or not made during the pendency of an application for reissue patent or a reexamination proceeding or both, shall not be accepted unless a certificate of correction under § 1.323 is requested by the patent owner which meets the terms of paragraphs (b) and (c) of this section.

(b) A request for certificate of correction under this section shall not be granted unless the certificate identifies:

(1) The accession number for the replacement or supplemental deposit;

(2) The date of the deposit; and

(3) The name and address of the depository.

(c) A request for a certificate of correction under this section shall not be granted unless the request is made promptly after the replacement or supplemental deposit has been made and:

(1) Includes a verified statement of the reason for making the replacement or supplemental deposit;

(2) Includes a verified statement from a person in a position to corroborate the fact, and shall state, that the replacement or supplemental deposit is of a biological material which is identical to that originally deposited;

(3) Includes a verified showing that the patent owner acted diligently

(i) In the case of a replacement deposit, in making the deposit after receiving notice that samples could no longer be furnished from an earlier deposit, or

(ii) In the case of a supplemental deposit, in making the deposit after receiving notice that the earlier deposit had become contaminated or had lost its capability to function as described in the specification;

(4) Includes a verified statement that the term of the replacement or supplemental deposit expires no earlier than the term of the deposit being replaced or supplemented; and

(5) Otherwise establishes compliance with these regulations, except that if the person making one or more of the required statements or showing is an attorney or agent registered to practice before the Office, that statement or showing need not be verified.

(d) A depositor s failure to replace a deposit, or in the case of a patent, to diligently replace a deposit and promptly thereafter request a certificate of correction which meets the terms of paragraphs (b) and (c) of this section, after being notified that the depository possessing the deposit cannot furnish samples thereof, shall cause the application or patent involved to be treated in any Office proceeding as if no deposit were made.

(e) In the event a deposit is replaced according to these regulations, the Office will apply a rebuttable presumption of identity between the original and the replacement deposit where a patent making reference to the deposit is relied upon during any Office proceeding.

(f) A replacement or supplemental deposit made during the pendency of an application for patent may be made for any reason.

(g) In no case is a replacement or supplemental deposit of a biological material necessary where the biological material, in accordance with § 1.802(b), need not be deposited.

(h) No replacement deposit of a biological material is necessary where a depository can furnish samples thereof but the depository for national security, health or environmental safety reasons is unable to provide samples to requesters outside of the jurisdiction where the depository is located.

(i) The Office will not recognize in any Office proceeding a replacement deposit of a biological material made by a patent owner where the depository could furnish samples of the deposit being replaced.

37 CFR 1.805 relates to the deposit of a biological material to replace or supplement a previous deposit. The term "replacement" is directed to those situations where one deposit is being substituted for another. An applicant may have greater latitude in replacing a deposit during the pendency of an application than after the patent is granted. Replacement will typically take place where the earlier deposit is no longer viable. The term "supplement" is directed to those situations where the earlier deposit is still viable in the sense that it is alive and capable of replication either directly or indirectly, but has lost a quality (e.g., purity, functionality) it allegedly possessed at the time the application was filed. The procedures in these rules contemplate that only the original depositor would have a right to replace or supplement the original deposit.

2407.01 In a Pending Application

37 CFR 1.805(a) relates to the procedure for replacing or supplementing a deposit with respect to a pending application or a patent. An applicant or patent owner is required to notify the Office when it obtains information that the depository possessing a deposit cannot furnish samples of the deposit to satisfy the requirements of 35 U.S.C. 112. When the Office is so informed or otherwise becomes aware that samples of the deposited material cannot be furnished by the depository, the examiner will treat the application or reexamination proceeding, whichever is applicable, as if no deposit existed. A replacement or supplemental deposit will be accepted if it meets all the requirements for making an original deposit.

It should be noted that in a pending application, an applicant need not replace the identical material previously deposited, but may make an original deposit of a

biological material which is specifically identified and described in the application as filed. Whether this alternative deposit will meet the requirements of 35 U.S.C. 112 with respect to the claimed subject matter must be resolved by the examiner on a case–by–case basis. The conditions in 37 CFR 1.802(b) and 37 CFR 1.804 (b) must be satisfied.

2407.02 After a Patent Has Issued

A replacement deposit made in connection with an application for reissue patent or a reexamination proceeding or both shall not be accepted unless a certificate of correction is requested which meets the terms of 37 CFR 1.805(b) and 37 CFR 1.805 (c) for replacement deposits. Any correction made to the original patent will be automatically incorporated into the reissued or reexamined patent unless changes are made during examination of the reissue application or reexamination proceeding.

37 CFR 1.805(b) and 37 CFR 1.805(c), specify the procedures that a patent owner may follow to ensure that a patent contains the appropriate information about a deposited biological material in the event that a replacement or supplemental deposit is made after the patent is granted. 37 CFR 1.805(b) describes the information which must be contained in the certificate of correction, whereas 37 CFR 1.805(c) de -scribes the information which must be provided in the request to make the correction.

2407.03 Failure to Replace

37 CFR 1.805(d) sets forth the Office position that the failure to make a replacement deposit in a case pending before the Office, for example a reissue or reexamination proceeding, where a deposit is considered to be necessary to satisfy the requirements of 35 U.S.C. 112, shall cause the application or patent involved to be treated in any Office proceeding as if no deposit were made. The provisions of 37 CFR 1.805(g) indicate that a replacement need not be made where, at the point in time when replacement would otherwise be necessary, access to the necessary biological material was otherwise available. For example, a replacement deposit would not be required under the circumstances where access to the necessary biological material was established through commercial suppliers.

2407.04 Treatment of Replacement

37 CFR 1.805(e) indicates that the Office will apply a rebuttable presumption of identity between the replacement deposit and an original deposit where a patent making reference to the deposit is relied on during any Office proceeding. This means that where a replacement deposit is permitted and made, the examiner will assume that the same material as described in the patent is accessible from the identified depository unless evidence to the contrary comes to the attention of the Office.

An applicant for patent may make a replacement deposit during the pendency of the application for any reason. The provisions of 37 CFR 1.805(f) recognize that since an original deposit may be made during the pendency of the application subject to the conditions of 37 CFR 1.809, a replacement deposit logically cannot be held to any higher standard or any further requirements.

2407.05 Exemption From Replacement

The provisions of 37 CFR 1.805(h) indicate that a replacement deposit is not required even though the depository cannot furnish samples, under certain conditions, to those requesting a sample outside of the jurisdiction where the depository is located. The conditions are specified in this paragraph as being limited to national security, health or environmental safety reasons.

2407.06 Replacement May Not Be Recognized

Finally, 37 CFR 1.805(i) indicates that the Office will not recognize in any Office proceeding a replacement deposit made by the patent owner where the depository could furnish samples of the original deposit being replaced. The best evidence of what was originally deposited should not be lost through destruction or replacement if made in association with an existing patent. A supplemental deposit may be accepted in an Office proceeding, however, depending on the circumstances in each case.

2408 Term of Deposit [R–1]

37 CFR 1.806 Term of deposit.

A deposit made before or during pendency of an application for patent shall be made for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposit was received by the depository. In any case, samples must be stored under agreements that would make them available beyond the enforceable life of the patent for which the deposit was made.

The term of deposit must satisfy the requirements of the Budapest Treaty which sets a term of at least 30 years from the date of deposit and at least five (5) years after the most recent request for the furnishing of a sample of the deposit was received by the depository. In the event that the 30–year term covers the 17–year term > or 20–year term < of the patent plus six (6) years to include the Statute of Limitations, no further requirement is necessary. Unless applicant indicates that the deposit has been made under the Budapest Treaty, applicant must indicate the term for which the deposit has been made. The mere possibility of patent term extension or extended litigation involving the patent should not be considered in this analysis.

In the event that the 30–year term of deposit measured from the date of deposit would necessarily terminate within the period of enforceability of the patent (the normal 17–year term >or 20–year term< plus six (6) years to include the Statute of Limitations), samples must be stored under agreements that would make them available beyond the enforceable life of the patent (i.e., until 23 > or 26 < years after issuance) for which the deposit was made. No requirement should be made as to any particular period of time beyond the enforceable life of the patent. The purpose of the requirement is to insure that a deposited biological material necessary for the practice of a patented invention would be available to the public after expiration of the patent for which the deposit was made. The term of the deposit must comply with the requirements of each sentence of 37 CFR 1.806 whether or not the deposit is made under the Budapest Treaty. A specific statement that the deposit complies with the second sentence of this section is required only where the 30–year term would terminate within the enforceable life of the patent.

2409 Viability of Deposit [R–3]

37 CFR 1.807. Viability of deposit.

(a) A deposit of biological material that is capable of self–replication either directly or indirectly must be viable at the time of deposit and during the term of deposit. ** Viability may be tested by the depository. The test must >conclude only that the deposited material is capable of< reproduction. No evidence is necessarily required regarding the ability of the deposited material to perform any function described in the patent application.

(b) A viability statement for each deposit of a biological material defined in paragraph (a) of this section not made under the Budapest Treaty on the International Recognition of the Deposit of Micro–organisms for the Purposes of Patent Procedure must be filed in the application and must contain:

(1) The name and address of the depository;

(2) The name and address of the depositor;

(3) The date of deposit;

(4) The identity of the deposit and the accession number given by the depository;

(5) The date of the viability test;

(6) The procedures used to obtain a sample if the test is not done by the depository; and

(7) A statement that the deposit is capable of reproduction.

(c) If a viability test indicates that the deposit is not viable upon receipt, or the examiner cannot, for scientific or other valid reasons, accept the statement of viability received from the applicant, the examiner shall proceed as if no deposit has been made. The examiner will accept the conclusion set forth in a viability statement issued by a depository recognized under § 1.803(a).

37 CFR 1.807 requires that the deposit of biological material that is capable of self–replication either directly or indirectly must be viable at the time of deposit and during the term of deposit. This requirement for viability is essentially a requirement that the deposited material is capable of reproduction. For the purpose of making a deposit under these rules, there is no requirement that evidence be provided that the deposited material is capable or has the ability to perform any function described in the patent application. However, as with any other issue of description or enablement, if the examiner has evidence or reason to question the objective statements made in the patent application, applicants may be required to demonstrate that the deposited biological material will perform in the manner described.

Under the Budapest Treaty, there is a requirement that the deposit be tested for viability before it is accepted. Thus, a mere statement by an applicant, an authorized representative of applicant or the assignee that the deposit has been accepted under the Budapest Treaty would satisfy 37 CFR 1.807.

For each deposit which is not made under the Budapest Treaty, a viability statement must be filed in the patent application and contain the information listed in paragraph (b) of this section. Under 37 CFR 1.807(c), the examiner will accept the conclusion set forth in a viability statement which is issued by a depository recognized under 37 CFR 1.803(a). If the viability test indicates that the deposit is not viable upon receipt, or the examiner cannot, for scientific or other valid reasons, accept the statement of viability received from the applicant, the examiner shall so notify the applicant stating the reasons for not accepting the statement and proceed with the examination process as if no deposit had been made.

2410 Furnishing of Samples

37 CFR 1.808 Furnishing of samples.

(a) A deposit must be made under conditions that assure that:

(1) Access to the deposit will be available during pendency of the patent application making reference to the deposit to one determined by the Commissioner to be entitled thereto under § 1.14 and 35 U.S.C. 122, and

(2) Subject to paragraph (b) of this section, all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of the patent.

(b) The depositor may contract with the depository to require that samples of a deposited biological material shall be furnished only if a request for a sample, during the term of the patent:

(1) Is in writing or other tangible form and dated;

(2) Contains the name and address of the requesting party and the accession number of the deposit; and

(3) Is communicated in writing by the depository to the depositor along with the date on which the sample was furnished and the name and address of the party to whom the sample was furnished.

(c) Upon request made to the Office, the Office will certify whether a deposit has been stated to have been made under conditions which make it available to the public as of the issue date of the patent grant provided the request contains:

(1) The name and address of the depository;

(2) The accession number given to the deposit;

(3) The patent number and issue date of the patent referring to the deposit; and

(4) The name and address of the requesting party.

2410.01 Conditions of Deposit

37 CFR 1.808 requires that the deposit of biological material be made under two (2) conditions:

(1) access to the deposit will be available during pendency of the patent application making reference to the deposit to one determined by the Commissioner to be entitled thereto under 37 CFR 1.14 and 35 U.S.C. 122, and

(2) with one exception, that all restrictions imposed by the depositor on the availability to the public of the deposited biological material be irrevocably removed upon the granting of the patent.

The one exception that is permitted is specified in 37 CFR 1.808(b)which permits the depositor to contract with the depository to require that samples of a deposited biological material shall be furnished only if a request for a sample, during the term of the patent, meets any one or all of the three conditions specified in this paragraph. These conditions are:

(1) the request is in writing or other tangible form and dated; and/or

(2) the request contains the name and address of the requesting party and the accession number of the deposit; and/or

(3) the request is communicated in writing by the depository to the depositor along with the date on which the sample was furnished and the name and address of the party to whom the sample was furnished.

It should be noted that this exception to the general rule that all restrictions will be removed must be strictly followed and that no variations of this explicit exception will be accepted as meeting the conditions of this section. Although this exception is consistent with the provisions in the Budapest Treaty and its implementing regulations (Rule 11.4), other conditions on accessibility are permitted under the Budapest Treaty as prescribed by national law. Consequently, the mere indication that a deposit has been made under conditions prescribed by the Budapest Treaty would satisfy all conditions of these regulations except the requirement that all restrictions on access be removed on grant of the patent. *Ex parte Hildebrand*, 15 USPQ2d 1662 (Bd Pat. App. & Int. 1990).

2410.02 Certification of Accessibility of Deposit

Since the mere description of a deposit or identity of a deposit in a patent specification is not necessarily an indication that a requirement for deposit was made or that a deposit which complies with these rules has been made, accessibility to a deposited material referenced in a patent may depend on the satisfaction of conditions not apparent on the face of the patent. For these reasons, and upon request made to the Patent and Trademark Office, the Office will certify whether a deposit has been stated to have been made under conditions which would make it available to the public as of the issue date of the patent grant provided the request is made to the Director of Patent Examining Group 1800, and contains the following information:

(1) the name and address of the depository;

(2) the accession number given to the deposit;

(3) the patent number and issue date of the patent referring to the deposit; and

(4) the name and address of the requesting party.

For those deposits made pursuant to the Budapest Treaty, the World Intellectual Property Organization provides a form (Form BP–12) for requesting a certification of the availability of samples of deposited micro–organisms pursuant to Rule 11.3(a) of the Regulations under the Budapest Treaty. Copies of this form are available from the Director of Patent Examining Group 1800.

2411 Examination Procedures

37 CFR 1.809. Examination procedures.

(a) The examiner shall determine pursuant to § 1.104 in each application for patent, application for reissue patent or reexamination proceeding if a deposit is needed, and if needed, if a deposit actually made is acceptable for patent purposes. If a deposit is needed and has not been made or replaced or supplemented in accordance with these regulations, the examiner, where appropriate, shall reject the affected claims under the appropriate provision of 35 U.S.C. 112, explaining why a deposit is needed and/or why a deposit actually made cannot be accepted.

(b) The applicant for patent or patent owner shall respond to a rejection under paragraph (a) of this section by—

(1) In the case of an applicant for patent, making an acceptable original or replacement or supplemental deposit or assuring the Office in writing that an acceptable deposit will be made on or before the date of payment of the issue fee, or, in the case of a patent owner, requesting a certificate of correction of the patent which meets the terms of paragraphs (b) and (c) of § 1.805, or

(2) Arguing why a deposit is not needed under the circumstances of the application or patent considered and/or why a deposit actually made should be accepted. Other replies to the examiner's action shall be considered non–responsive. The rejection will be repeated until either paragraph (b)(1) of this section is satisfied or the examiner is convinced that a deposit is not needed.

(c) If an application for patent is otherwise in condition for allowance except for a needed deposit and the Office has received a written assurance that an acceptable deposit will be made on or before payment of the issue fee, the Office will mail to the applicant a Notice of Allowance and Issue Fee Due together with a requirement that the needed deposit be made within three months. The period for satisfying this requirement is extendible under § 1.136. Failure to make the needed deposit in accordance with this requirement will result in abandonment of the application for failure to prosecute.

(d) For each deposit made pursuant to these regulations, the specification shall contain:

(1) The accession number for the deposit;

(2) The date of the deposit;

(3) A description of the deposited biological material sufficient to specifically identify it and to permit examination; and

(4) The name and address of the depository.

37 CFR 1.809 sets forth procedures that will be used by the examiner to address a deposit issue. The burden is initially on the Office to establish that access to a biological material is necessary for the satisfaction of the statutory requirements for patentability under 35 U.S.C. 112. Once the Office has met this burden, the burden shifts to the applicant or patent owner to demonstrate that access to such biological material either is not necessary or is, either, already available or that a deposit of such material will be made in accordance with these regulations.

2411.01 Rejections Based on Deposit Issue

Under 37 CFR 1.809(a), once the examiner has determined that access to a biological material is necessary, and there is no information that would support the conclusion that access is currently available in accordance with these regulations, the examiner should make an appropriate rejection under 35 U.S.C. 112 until such time as a deposit in accordance with these regulations is actually made or a written assurance is received in the patent application that such a deposit will be made upon an indication of allowability of the application. The examiner should clearly indicate the statutory basis for the rejection and the reasons that are relied upon by the examiner to conclude that the application does not comply with some requirement of 35 U.S.C. 112. Although not exhaustive, the following grounds of rejection may be applicable in appropriate circumstances:

(1) 35 U.S.C. 112, first paragraph – lack of an enabling disclosure without access to a specific biological material. This ground of rejection should be accompanied by evidence of scientific reasoning to support the conclusion that a person skilled in the art could not make or use the invention defined in and commensurate with the claims without access to the specific biological material.

(2) 35 U.S.C. 112, first paragraph – description requirement. This ground of rejection typically arises in the context that the application as filed does not contain a description to support an amendment to the specification or claims. An amendment to the claims that is not described in the application as filed would justify a rejection of the affected claims under 35 U.S.C. 112, first paragraph. If an amendment is made to the application, other than the claims, that is not described in the application as filed, this would justify an objection under 35 U.S.C. 112, first paragraph and/or 35 U.S.C. 132 (prohibition against the introduction of new matter) and a requirement that the amendment be canceled.

(3) 35 U.S.C. 112, first paragraph – best mode requirement. This ground of rejection will be rare in the ex parte examination process because it requires (i) a finding by the examiner that, at the time the application was filed, the inventor(s) knew of a specific material that

was considered by the inventor(s) to be better than any other, and (ii) if a best mode was contemplated at that time, that the inventor(s) concealed the best mode (accidentally or intentionally) by failing to adequately describe that best mode. See *Chemcast Corp.* v. *Arco Industries Corp.*, 913 F.2d 923, 16 USPQ2d 1033 (Fed. Cir. 1990). The Court of Appeals for the Federal Circuit has twice resolved a best mode issue arising in the context of a biotechnology invention in favor of the patentee. See *Scripps Clinic and Research Foundation* v. *Genentech Inc.*, 927 F.2d 1565, 18 USPQ2d 1001 (Fed. Cir. 1991) with respect to monoclonal antibodies, and *Amgen Inc.* v. *Chugai Pharmaceutical Co. Ltd.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991) with respect to mammalian host cells.

(4) 35 U.S.C. 112, second paragraph – indefiniteness. This ground of rejection, as applied to a deposit issue, requires the examiner to provide reasons why the terms in the claims and/or scope of the invention are unclear because of an incomplete or inaccurate description or the absence of a reference to a biological material.

(5) 35 U.S.C. 112, second paragraph – claims do not set forth what applicants regard as their invention. This ground of rejection requires the citation of some evidence, not contained in the application as filed, that the claims do not set forth what applicants regard as their invention. *In re Prater*, 415 F.2d 1393, 162 USPQ 541 (CCPA 1969). Any disagreement between the content of the application disclosure and the scope of the claims should be addressed under 35 U.S.C. 112, first paragraph. See *In re Ehrreich*, 590 F.2d 902, 200 USPQ 504 (CCPA 1979).

Where a deposit is required to satisfy 35 U.S.C. 112, a deposit must be made in accordance with these regulations. A deposit accepted in any IDA under the Budapest Treaty shall be accepted for patent purposes if made under conditions which comply with 37 CFR 1.806 and 37 CFR 1.808(a) concerning term of deposit and permissible conditions on access once the patent is granted.

2411.02 Responses to Rejections Based on Deposit Issue

Once a rejection under 35 U.S.C. 112 has been made by the examiner directed to the absence of access to a biological material, applicant may respond, pursuant to 37 CFR 1.809 (b)(1), by either making an acceptable original or replacement deposit in accordance with these regulations, or assuring the Office in writing that an acceptable deposit will be made on or before the date of payment of the issue fee, or by submitting an argument of why a deposit is not required under the circumstances of the application being considered. Other replies to such a rejection by the examiner shall be considered non–responsive and may result in abandonment of the application. The rejection will be repeated and made final until the requirements of 37 CFR 1.809(b)(1) are satisfied or the examiner is convinced that a deposit is not required for the claimed subject matter. Once the rejection is made final, the requirements of 37 CFR 1.116 apply to further submissions. The written assurance will be accepted by the Office if it clearly states that an acceptable deposit will be made within the required time and under conditions which satisfy these rules. In the case that an acceptable written assurance has been made by the applicant, the rejection under 35 U.S.C 112 directed to the absence of access to the biological material should be removed.

2411.03 Application in Condition for Allowance Except for Deposit

As set forth in 37 CFR 1.809(c), in the event that an application for patent is otherwise in condition for allowance except for a required deposit and the Office has received a written assurance that an acceptable deposit will be made, the Office will mail to the applicant a requirement that the required deposit be made within three (3) months together with the Notice of Allowance and Issue Fee Due. Although the period for paying the issue fee cannot be extended under the provisions of 37 CFR 1.136, the period for satisfying the requirement to make an acceptable deposit may be extended under the provisions of that section. Failure to make the needed deposit in accordance with this requirement may be considered a failure to prosecute the application under 35 U.S.C. 133 and result in abandonment of the application. Once the deposit has been made, information regarding the deposit, such as the name of the depository, the accession number and the date of the deposit, that is to be added to the specification must be added by means of filing an amendment under the provisions of 37 CFR 1.312. A petition and fee are required if the 37 CFR 1.312 amendment is filed after the issue fee has been paid.

2411.04 After a Patent Has Been Granted

In a proceeding involving a patent, it may not be possible to request a certificate of correction of the patent which meets the terms of 37 CFR 1.805(b) and 37 CFR 1.805(c). For example, if the patent owner is on notice that samples of an original deposit can no longer be furnished by the depository, failure to diligently make a replacement deposit will preclude grant of a certificate of correction. A replacement deposit subsequently made will not be recognized by the Office nor will a request for certificate of correction, even if made promptly thereafter, be granted. It would also not be possible to request a certificate of correction of the patent which meets the terms of 37 CFR 1.805(b) and 37 CFR 1.805(c) where no original deposit was made before or during the pendency of the application which matured into the patent.

A patent defective because of lack of a necessary deposit is necessarily fatally defective for failure to comply with the first paragraph of 35 U.S.C. 112. Reissue is not available in such cases. See *In re Hay*, 534 F.2d 917, 189 USPQ 790 (CCPA 1976). Whether reissue is available where a biological material necessary for compliance with 35 U.S.C. 112 was known and readily available at the time of issuance of the patent and subsequently ceased to be readily available is problematic. Nevertheless, the rules do not provide for post-issuance original deposits.

Where an applicant for patent has any doubt as to whether access to a biological material specifically identified in the specification is necessary to satisfy 35 U.S.C. 112 or whether such a material, while currently freely available, may become unavailable in the future, the applicant would be well-advised to make a deposit thereof before any patent issues. Similarly, where a patent owner has any doubt whether a deposit referred to in the specification is a biological material necessary to satisfy 35 U.S.C. 112 and, if the material is necessary, whether it is otherwise known and readily available, the patent owner would be well-advised to follow the procedures set forth in 37 CFR 1.805(b) and 37 CFR 1.805(c) after receiving the notice specified in those paragraphs.

2411.05 Content of Application with Respect to Deposited Material

37 CFR 1.809(d) sets forth the requirements for the content of the specification with respect to a deposited biological material. Specifically, the specification shall contain the accession number for the deposit, the date of the deposit, the name and address of the depository, and a description of the deposited biological material sufficient to specifically identify it and to permit examination. The description also must be sufficient to permit verification that the deposited biological material is in fact that disclosed. Once the patent issues, the description must be sufficient to aid in the resolution of questions of infringement. As a general rule, the more information that is provided about a particular deposited biological material, the better the examiner will be able to compare the identity and characteristics of the deposited biological material with the prior art.

2420 The Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures – the Sequence Rules

Prior to the effective date (October 1, 1990) and implementation of the sequence rules (37 CFR 1.821 through 1.825), applications for patents that included nucleotide or amino acid sequence information posed special problems for the Office. While not related to the disclosure requirements of an invention, problems existed in the presentation, examination and printing of nucleotide and amino acid sequence data that appeared in patent applications because of the lack of uniformity in submission of sequence data to the Office and the impracticality of properly searching and examining sequences submitted in paper form. In summary, the diversity and complexity of nucleotide and amino acid sequence data resulted in searching and analysis difficulties both within the Office and outside the Office, decreased accuracy of search and reproduction and increased costs. These difficulties made the development and implementation of the sequence rules a critical necessity for the Office. As such, the Office amended its regulations to establish a standardized format for descriptions of nucleotide and amino acid sequence data submitted as a part of patent applications, in conjunction with the required submission of that data in computer readable form. The final rules were published in the *Federal Register* at 55 FR 18230 (May 1, 1990) and in the *Official Gazette* at 1114 O.G. 29 (May 15, 1990). The sequence rules went into effect on October 1, 1990.

2421 Overview of the Sequence Rules

2421.01 Applications Affected

The sequence rules require the use of standard symbols and a standard format for sequence data in most sequence–type patent applications. They further require the submission of that data in computer readable form. Compliance is required for most disclosures of sequence data in new applications. For the purpose of the sequence rules, the term "new" with regard to applications means:

– For regular US applications, the application must have been filed on or after October 1, 1990. Continuing applications that claim a date prior to October 1, 1990, under 35 U.S.C. 120, except continuations–in–part (CIPs) filed on or after October 1, 1990, where material added includes a sequence, are not new applications.

– For PCT applications, the international filing date must be on or after October 1, 1990, and the US must be one of the designated states and the US must be the International Searching Authority and/or the International Preliminary Examining Authority. For national stage applications, the international filing date, not the 371 date, is used. For international applications, the international filing date, not the U.S. or foreign priority date, is used.

– Not applicable to reissues or reexams filed after October 1, 1990, unless application which matured into patent was also subject to rules.

– Not applicable to continuations or divisionals filed after October 1, 1990, unless parent application was also subject to rules.

– Will apply to CIPs where parent application subject to rules or where new material includes sequence information that falls within rules. Where a CIP is filed on or after October 1, 1990, and claims the benefit of a filing date prior to October 1, 1990, under 35 U.S.C. 120 and material added includes a sequence, the requirement for compliance is limited to the newly added sequence material. Full compliance, for all sequence information in the CIP is, however, encouraged.

The Office encourages voluntary compliance for applications not subject to rules, but all aspects of the rules must be complied with before data will be entered into the database. This includes submission of all statements required by the rules. In exceptional circumstances, it should be noted that the Office may waive the rules via a 37 CFR 1.183 petition.

2421.02 Summary of the Requirements of the Sequence Rules

Basically, the sequence rules define a set of symbols and procedures that are both mandatory and the only way that an applicant is permitted to describe information about a sequence that falls within the definitions used in the rules. Thus, 37 CFR 1.821 of the rules defines a sequence for the purpose of the rules, the requirements for specific symbols, formats, paper and computer readable copies of the sequence, and the deadlines for complying with the requirements. 37 CFR 1.822 to 37 CFR 1.824 set forth detailed descriptions of the requirements that are mandatory for the presentation of sequence data, and 37 CFR 1.825 sets forth procedures that are available to an applicant in the event that amendments to the sequence information or replacement of the computer readable copy become necessary.

The sequence rules embrace all unbranched nucleotide sequences with ten or more bases and all unbranched, non–D amino acid sequences with four or more amino acids. The rules apply to all sequences in a given application, whether claimed or not. All such sequences are relevant for the purposes of building a comprehensive database and properly assessing prior art. It is therefore essential that all sequences, whether only disclosed or also claimed, be included in the database.

2421.03 Notification of a Failure to Comply

With respect to the Office's determination of compliance with the sequence rules and the opportunities afforded applicants to satisfy the requirements of the rules, applicants will be notified of easily detectable deficiencies early in the application process. Deficiencies of a more sophisticated nature will likely only be detected by the examiner to whom the application is assigned. Applicants whose computer readable forms are damaged in the mail, are not readable, or are missing mandatory elements will be notified shortly after receipt of the application by the Office. Other errors or inconsistencies will be noted by the examiner early in the examination process. Upon detection of damage or a deficiency, a notice will be sent to the applicant detailing the damage or deficiency and setting at least a one month period for response. The period for response will usually be one month. However, if the notice is sent out with an Office communication having a longer period for response, the period for response may be longer than one month, e.g.,

where the notice is sent with an Office action on the merits setting a three month period for response. Extensions of time in which to reply will be available pursuant to 37 CFR 1.136. When an action by the applicant, such as a response to a notice to comply from the Office, is determined to be a bona fide attempt to comply with the rules and it is apparent that compliance with some requirement has inadvertently been omitted, the opportunity to explain and supply the omission will be given before the question of abandonment will be considered. See 37 CFR 1.135(c). The relevant form paragraphs and a copy of the Notice to Comply to be used in applications subject to the sequence rules are included in MPEP § 2427 Form Paragraphs and Notice to Comply.

A notification of a failure to comply with the sequence rules will usually be accompanied by an analysis of a submitted computer readable form. Any inquiries regarding a specific computer readable form that has been processed by the Office should be directed to the Systems Branch of the Biotechnology Division of the Scientific and Technical Information Center.

2421.04 Future Changes to the Sequence Rules

With general regard to the symbols and format to be used for nucleotide and/or amino acid sequence data set forth in 37 CFR 1.822 and the form and format for sequence submissions in computer readable form set forth in 37 CFR 1.824, the Office intends to accommodate progress in the areas of both standardization and computerization as they relate to sequence data by subsequently amending the rules to take into account any such progress. This progress will probably be reflected in the refinement of or liberalization of the rules. For example, progress in the area of the standardization of sequence data will likely result in a more comprehensive rule. For example, the D–amino acids and branched sequences that are currently excluded from the rule may, in the future, be brought within the scope of the rule once the necessary standardization technology becomes available. As a further example, the computer readable form is currently limited to diskettes and tapes, but it can readily be seen that progress in the technology for developing databases of the type the Office has envisioned will likely permit a broadening of the permissible types of computer readable forms that may be submitted. The same can be said for the computer/operating–system configurations that are currently permitted by the rules. As the Office becomes able to provide greater refinement and liberality in these areas, the Office will do so by the publication of notices in the *Official Gazette* or formal rulemaking proposals, as appropriate.

2422 Nucleotide and/or Amino Acid Sequence Disclosures in Patent Applications

37 CFR 1.821. Nucleotide and/or amino acid sequence disclosures in patent applications.

(a) "Nucleotide and/or amino acid sequences" as used in §§ 1.821 through 1.825 is interpreted to mean an unbranched sequence of four or more amino acids or an unbranched sequence of ten or more nucleotides. Branched sequences are specifically excluded from this definition. Nucleotides and amino acids are further defined as follows:

(1) "Nucleotides" are intended to embrace only those nucleotides that can be represented using the symbols set forth in § 1.822(b)(1). Modifications, e.g., methylated bases, may be described as set forth in § 1.822(b), but shall not be shown explicitly in the nucleotide sequence.

(2) "Amino acids" are those L–amino acids commonly found in naturally occurring proteins and are listed in § 1.822(b)(2). Those amino acid sequences containing D–amino acids are not intended to be embraced by this definition. Any amino acid sequence that contains post–translationally modified amino acids may be described as the amino acid sequence that is initially translated using the symbols shown in § 1.822(b)(2) with the modified positions, e.g., hydroxylations or glycosylations, being described as set forth in § 1. 822(b), but these modifications shall not be shown explicitly in the amino acid sequence. Any peptide or protein that can be expressed as a sequence using the symbols in § 1.822(b)(2) in conjunction with a description elsewhere in the "Sequence Listing" to describe, for example, modified linkages, cross links and end caps, non–peptidyl bonds, etc., is embraced by this definition.

(b) Patent applications which contain disclosures of nucleotide and/or amino acid sequences, in accordance with the definition in paragraph (a) of this section, shall, with regard to the manner in which the nucleotide and/or amino acid sequences are presented and described, conform exclusively to the requirements of §§ 1.821 through 1.825.

(c) Patent applications which contain disclosures of nucleotide and/or amino acid sequences must contain, as a separate part of the disclosure on paper copy, hereinafter referred to as the "Sequence Listing," a disclosure of the nucleotide and/or amino acid sequences and associated information using the symbols and format in accordance with the requirements of §§ 1.822 and 1.823. Each sequence disclosed must appear separately in the "Sequence Listing." Each sequence set forth in the "Sequence Listing" shall be assigned a separate identifier written as SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, etc.

(d) Where the description or claims of a patent application discuss a sequence listing that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the assigned identifier, in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

(e) A copy of the "Sequence Listing" referred to in paragraph (c) of this section must also be submitted in computer readable form in accordance with the requirements of § 1.824. The computer readable form is a copy of the "Sequence Listing" and will not necessarily be retained as part of the patent application file. If the computer readable

form of a new application is to be identical with the computer readable form of another application of the applicant on file in the Office, reference may be made to the other application and computer readable form in lieu of filing a duplicate computer readable form in the new application. The new application shall be accompanied by a letter making such reference to the other application and computer readable form, both of which shall be completely identified.

(f) In addition to the paper copy required by paragraph (c) of this section and the computer readable form required by paragraph (e) of this section, a statement that the content of the paper and computer readable copies are the same must be submitted with the computer readable form. Such a statement must be a verified statement if made by a person not registered to practice before the Office.

(g)If any of the requirements of paragraphs (b) through (f) of this section are not satisfied at the time of filing under 35 U.S.C. 111 or at the time of entering the national stage under 35 U.S.C. 371, applicant has one month from the date of a notice which will be sent requiring compliance with the requirements in order to prevent abandonment of the application. Any submission in response to a requirement under this paragraph must be accompanied by a statement that the submission includes no new matter. Such a statement must be a verified statement if made by a person not registered to practice before the Office.

(h)If any of the requirements of paragraphs (b) through (f) of this section are not satisfied at the time of filing, in the United States Receiving Office, an international application under the Patent Cooperation Treaty (PCT) applicant has one month from the date of a notice which will be sent requiring compliance with the requirements, or such other time as may be set by the Commissioner, in which to comply. Any submission in response to a requirement under this paragraph must be accompanied by a statement that the submission does not include new matter or go beyond the disclosure in the international application as filed. Such a statement must be a verified statement if made by a person not registered to practice before the Office.

(i) Neither the presence nor the absence of information which is not required under §§ 1.821 through 1.825, in an application shall create any presumption that such information is necessary to satisfy one or more of the requirements of 35 U.S.C.112. Further, the grant of a patent on an application that is subject to the requirements of §§ 1.821 through 1.825 shall constitute a conclusive presumption that said patent complies with the requirements of §§ 1.821 through 1.825.

(j) Envelopes containing only application papers, computer readable forms and fees filed under this section should be marked "Box SEQUENCE."

2422.01 Definitions of Nucleotide and/or Amino Acids for Purpose of Sequence Rules

37 CFR 1.821(a) presents a definition for "nucleotide and/or amino acid sequences." This definition sets forth limits, in terms of numbers of amino acids and/or numbers of nucleotides, at or above which compliance with the sequence rules is required. Further, compliance with the sequence rules is only required for unbranched sequences. Branched sequences are explicitly excluded from the scope of the sequence rules. The limit of four or more amino acids was established for consistency with limits in place for industry database collections whereas the limit of ten or more nucleotides, while lower than certain industry database limits, was established to encompass those nucleotide sequences to which the smallest probe will bind in a stable manner. The limits for amino acids and nucleotides are also consistent with those established for sequence data exchange with the Japanese Patent Office and the European Patent Office.

37 CFR 1.821(a)(1) and 37 CFR 1.821(a)(2) present further definitions for those nucleotide and amino acid sequences that are intended to be embraced by the sequence rules. Situations in which the applicability of the rules are in issue will be resolved on a case−by−case basis.

Nucleotide sequences are further limited to those that can be represented by the symbols set forth in 37 CFR 1.822(b)(1). The presence of other than typical 5' to 3' phosphodiester linkages in a nucleotide sequence does not render the rules inapplicable. The Office does not want to exclude linkages of the type commonly found in naturally occurring nucleotides, e.g., eukaryotic end capped sequences.

Amino acid sequences are further limited to those listed in 37 CFR 1.822(b)(2) and those L−amino acids that are commonly found in naturally occurring proteins. The limitation to L−amino acids is based upon the fact that there currently exists no widely accepted standard nomenclature for representing the scope of amino acids encompassed by non−L−amino acids, and, as such, the process of meaningfully encoding these other amino acids for computerized searching and printing is not currently feasible. The presence of one or more D−amino acids in a sequence will exclude that sequence from the scope of the rules. (Voluntary compliance is, however, encouraged in these situations; the symbol "Xaa" can be used to represent D−amino acids.) The sequence rules embrace "[a]ny peptide or protein that can be expressed as a sequence using the symbols in 37 CFR 1.822(b)(2) in conjunction with a description elsewhere in the "Sequence Listing" to describe, e.g., modified linkages, cross links, end caps, non−peptidyl bonds, etc." 37 CFR 1.821(a)(2).

With regard to amino acid sequences, the use of the terms "peptide or protein" implies, however, that the amino acids in a given sequence are linked by at least three consecutive peptide bonds. Accordingly, an amino acid sequence is not excluded from the scope of the rules merely due to the presence of a single non−peptidyl

bond. If an amino acid sequence can be represented by a string of amino acid abbreviations, with reference, where necessary, to a features table to explain modifications in the sequence, the sequence comes within the scope of the rules. However, the rules are not intended to encompass the subject matter that is generally referred to as synthetic resins.

2422.02 The Requirement for Exclusive Conformance; Sequences Presented in Drawing Figures

37 CFR 1.821(b) requires exclusive conformance, with regard to the manner in which the nucleotide and/or amino acid sequences are presented and described, with the sequence rules for all applications that include nucleotide and amino acid sequences that fall within the definitions. This requirement is necessary to minimize any confusion that could result if more than one format for representing sequence data was employed in a given application. It is also expected that the required standard format will be more readily and widely accepted and adopted if its use is exclusive, as well as mandatory.

In view of the fact that many significant sequence characteristics may only be demonstrated by a figure, the exclusive conformance requirement of this section may be relaxed for drawing figures. This is especially true in view of the fact that the representation of double stranded nucleotides is not permitted in the "Sequence Listing" and many significant nucleotide features, such as "sticky ends" and the like, will only be shown effectively by reference to a drawing figure. Further, the similarity or homology between/among sequences can only be depicted in an effective manner in a drawing figure. Similarly, drawing figures are recommended for use with amino acid sequences to depict structural features of the corresponding protein, such as finger regions and Kringle regions. The situations discussed herein are given by way of example only and there may be many other reasons for relaxing the requirements of this section for the drawing figures. It should be noted, though, that when a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence indentifer ("SEQ ID NO:X") must be used, either, in the drawing or in the Brief Description of the Drawings.

2422.03 The Requirements for a Sequence Listing and Sequence Identifiers; Sequences Embedded in Application Text; Variants of a Presented Sequence

37 CFR 1.821(c) requires that applications containing nucleotide and/or amino acid sequences that fall within the above definitions, contain, as a separate part of the disclosure on paper copy, a disclosure of the nucleotide and/or amino acid sequences, and associated information, using the format and symbols that are set forth in 37 CFR 1.822 and 37 CFR 1.823. This separate part of the disclosure, beginning on a new page within the specification, is referred to as the "Sequence Listing," and requires that each sequence disclosed in the application appear separately in the "Sequence Listing," with each sequence further being assigned a sequence identification number, referred to as "SEQ ID NO." A plurality of sequences may, if feasible, be presented on a single page, and this may be extended to the separate presentation of both nucleotide and amino acid sequences on the same page. The requirement for sequence identification numbers, at a minimum, requires that each sequence be assigned a different number for purposes of identification. However, where practical and for ease of reference, sequences should be presented in the separate part of the application in numerical order and in the order in which they are discussed in the application.

The requirement for compliance in 37 CFR 1.821(c) is directed to "disclosures of nucleotide and/or amino acid sequences." (Emphasis added.) All sequence information, whether claimed or not, that meets the length thresholds in 37 CFR 1.821(a) is subject to the rules. The goal of the Office is to build a comprehensive database that can be used for, inter alia, the purpose of assessing the prior art. It is therefore essential that all sequence information, whether only disclosed or also claimed, be included in the database. In those instances in which prior art sequences are only referred to in a given application by name and a publication or accession reference, they need not be included as part of the "Sequence Listing," unless an examiner considers the referred–to sequence to be "essential material," per MPEP § 608.01(p). However, if the applicant presents the sequence as a string of particular bases or amino acids, it is necessary to include the sequence in the "Sequence

Listing," regardless of whether the applicant considers the sequence to be prior art. In general, any sequence that is disclosed and/or claimed as a sequence, i.e., as a string of particular bases or amino acids, and that otherwise meets the criteria of 37 CFR 1.821(a), must be set forth in the "Sequence Listing."

It is generally acceptable to present a single, general sequence in accordance with the sequence rules and to discuss and/or claim variants of that general sequence without presenting each variant as a separate sequence in the "Sequence Listing." By way of example only, the following types of sequence disclosures would be treated as noted herein by the Office. With respect to "conservatively modified variants thereof" of a sequence, the sequences may be described as SEQ ID NO:X and "conservatively modified variants thereof," if desired. With respect to a sequence that "may be deleted at the C–terminus by 1, 2, 3, 4, or 5 residues," all of the implied variations do not need to be included in the "Sequence Listing." If such a situation were encompassed by the rules, it would introduce far too much complexity into the "Sequence Listing" and the Office's database. The possible mathematical variations that could result from this type of language could reasonably require a "Sequence Listing" that would be thousands of pages in length. In this latter example, only the undeleted sequence needs to be included in the "Sequence Listing," and the sequences may be described as SEQ ID NO:X from which deletions have been made at the C–terminus by 1, 2, 3, 4, or 5 residues. The Office's database will only contain the undeleted sequence.

37 CFR 1.821(d) requires the use of the assigned sequence identifier in all instances where the description or claims of a patent application discuss sequences regardless of whether a given sequence is also embedded in the text of the description or claims of an application. This requirement is also intended to permit references, in both the description and claims, to sequences set forth in the "Sequence Listing" by the use of assigned sequence identifiers without repeating the sequence in the text of the description or claims. Sequence identifiers can also be used to discuss and/or claim parts or fragments of a properly presented sequence. For example, language such as "residues 14 to 243 of SEQ ID NO:23" is permissible and the fragment need not be separately presented in the "Sequence Listing." Where a sequence is embedded in the text of an application, it must be presented in a manner that complies with the requirements of the sequence rules.

The rules do not alter, in any way, the requirements of 35 U.S.C. 112. The implementation of the rules has had no effect on disclosure and/or claiming requirements. The rules, in general, or the use of sequence identifiers throughout the specification and claims, specifically, should not raise any issues under 35 U.S.C. 112, first or second paragraphs. The use of sequence identification numbers (SEQ ID NO:X) only provides a shorthand way for applicants to discuss and claim their inventions. These identification numbers do not in any way restrict the manner in which an invention can be claimed.

2422.04 The Requirement for a Computer Readable Copy of the Official Paper Copy of the Sequence Listing

37 CFR 1.821(e) requires the submission of a copy of the "Sequence Listing" in computer readable form. The infor mation on the computer readable form will be entered into the Office's database for searching and printing nucleotide and amino acid sequences. This electronic database will also enable the Office to exchange patented sequence data, in electronic form, with the Japanese Patent Office and the European Patent Office. It should be noted that the Office's database complies with the confidentiality requirement imposed by 35 U.S.C. 122. Pending application sequences are maintained in the database separately from published or patented sequences. That is, the Office will not exchange or make public any information on any sequence until the patent application containing that information is published or matures into a patent, or as otherwise allowed by 35 U.S.C. 122.

The second sentence of 37 CFR 1.821(e) indicates that, as between the paper copy of the "Sequence Listing" and the computer readable copy thereof, the paper copy serves as the official copy. However, the Office may permit correction of the paper copy, at the least, during the pendency of a given application by reference to the computer readable copy thereof if both the paper and computer readable forms were submitted at the time of filing of the application and the totality of the circumstances otherwise substantiate the proposed correction. A mere discrepancy between the paper copy and the computer readable form may not, in and of itself, be sufficient to justify a proposed correction. In this regard, the Office will assume that the computer readable form

has been incorporated by reference into the application when the paper and computer readable forms were submitted at the time of filing of the application. The Office will attempt to accommodate or address all correction issues, but it must be kept in mind that the real burden rests with the applicant to ensure that any discrepancies between the paper copy and the computer readable form are eliminated or minimized. Applicants should be aware that there will be instances where the applicant may have to suffer the conserquences of any discrepancies between the two. All corrections will be made by appropriate fee–paid petitions. The paper copy also serves as the official copy for priority purposes. The Office does not desire to be bound by a requirement to permanently preserve computer readable forms for support, priority or correction purposes. For example, the Office will make corrections, where appropriate, by reference to the computer readable form as long as the computer readable form is still available to the Office. However, once use to the Office for processing has ended, i.e., once the Office has entered the data contained on the computer readable form into the appropriate database, the Office does not intend to further preserve the computer readable form submitted by the applicant.

2422.05 Reference to Previously Filed Identical Computer Readable Form; Continuing or Derivative Applications; Request for Transfer of Computer Readable Form

The last two sentences of 37 CFR 1.821(e) set forth the procedure to be followed when a computer readable form of a given application is identical with a computer readable form of another application. In that situation, an applicant may make reference to the other application and computer readable form therein in lieu of filing a duplicate computer readable form in the given application. That is, additional computer readable forms will not be required in derivative or continuing applications if the sequence information is exactly the same, i.e., with no additions or deletions, as that in a parent or previously filed application in which a complying computer readable form had been filed. If sequence information is deleted from or added to that submitted in a previously filed application, the procedure in this paragraph is not available and a new computer readable form is required. To take advantage of the procedure outlined in this section, applicants must request that the previously submitted sequence information be used in the given application in much the same manner as applicants must now request the transfer of drawings in derivative or continuing applications. A letter must be submitted in the given application requesting use of the previously filed sequence information. The letter must completely identify the other application, by application number, and the computer readable form, by indicating whether it was the only computer readable form filed in that application or whether it was the second, or subsequent, computer readable form filed.

2422.06 Requirement for Statement Regarding Content of Paper and Computer Readable Copies of Sequence Listing

37 CFR 1.821(f) requires that the paper and computer readable copies of the "Sequence Listing" be accompanied by a statement that the content of the paper and computer readable copies are the same, at the time when the computer readable form is submitted. This statement must be a verified statement if it is made by a person not registered to practice before the Office. Such a statement may be made by the applicant. See MPEP § 2428 for further information and Sample Statements.

2422.07 Requirements for Compliance, Statements Regarding New Matter, and Sanctions for Failure to Comply [R–1]

37 CFR 1.821(g) requires compliance with the requirements of 37 CFR 1.821(b) through (f), as discussed above, if they are not satisfied at the time of filing under 35 U.S.C. 111 >(a)< or at the time of entering the national stage of an international application under 35 U.S.C. 371, within one month from the date of a notice requiring compliance. > Applications filed under 35 U.S.C. 111(b) need not comply with 37 CFR 1.821 through 1.825, however, applicants are encouraged to file a Sequence Listing as defined in 37 CFR 1.821(c) for ease of identification of the sequence information contained in the provisional application. < Failure to comply will result in the abandonment of the application. The time period for response may be longer than one month if coupled with a different Office requirement. Submissions in response to requirements under this

paragraph must be accompanied by a statement that the submission includes no new matter. This statement must be a verified statement if made by a person not registered to practice before the Office. Again, such a statement may be made by the applicant. Extensions of time in which to reply to a requirement under this paragraph are available pursuant to 37 CFR 1.136. When an action by the applicant is a bona fide attempt to comply with these rules and it is apparent that compliance with some requirement has inadvertently been omitted, the opportunity to explain and supply the omission will be given before the question of abandonment is considered. See 37 CFR 1.135(c).

37 CFR 1.821(h) requires compliance with the requirements of 37 CFR 1.821(b) through (f), as discussed above, within one month from the date of a notice requiring compliance in an international application filed in the United States Receiving Office under the Patent Cooperation Treaty (PCT), if the above noted requirements are not satisfied at the time of filing. Submissions in response to requirements under this paragraph must be accompanied by a statement that the submission does not include new matter or go beyond the disclosure in the international application as filed. This statement must be a verified statement if made by a person not registered to practice before the Office. Such a statement may be made by an applicant. International applications that fail to comply with any of the requirements of 37 CFR 1.821(b) – (f) will be searched to the extent possible without the benefit of the information in computer readable form.

The requirement to submit a statement that a submission in response to the requirements of this section does not include new matter or go beyond the disclosure in the application as filed is not the first instance in which the applicant has been required to ensure that there is not new matter upon amendment. The requirement is analogous to that found in 37 CFR 1.125 regarding substitute specifications. When a substitute specification is required because the number or nature of amendments would make it difficult to examine the application, the applicant must include a statement that the substitute specification includes no new matter. The necessity of requiring a substitute "Sequence Listing," or pages thereof, is similar to the necessity of requiring a substitute specification and, likewise, the burden is on the applicant to ensure that no new matter is added. Applicants have a duty to comply with the statutory prohibition (35 U.S.C. 132 and 35 U.S.C. 251) against the introduction of new matter.

It should be noted that the treatment accorded errors in sequencing or any other errors prior to the implementation date of the sequence rules will be no different for those applications filed on or after the implementation date of these rules. The correction of errors in sequencing or any other errors that are made in describing an invention are, as they have always been, subject to the statutory prohibition (35 U.S.C. 132 and 35 U.S.C. 251) against the introduction of new matter.

2422.08 Presumptions Regarding Compliance

37 CFR 1.821(i) makes clear that neither the presence nor absence of information which is not required under the sequence rules will create a presumption that such information is necessary to satisfy any of the requirements of 35 U.S.C. 112. Further, this paragraph states that the grant of a patent on an application that is subject to 37 CFR 1.821 through 37 CFR 1.825 constitutes a conclusive presumption that the granted patent complies with the requirements of these rules. This paragraph addresses the concerns with respect to the weight that may ultimately be accorded an omission of an item of information which is not required under the rule, regardless of whether that item has been designated as "recommended" or "optional."

2422.09 Box Sequence; Hand Delivery of Sequence Listings and Computer Readable Forms

37 CFR 1.821(j) was included to facilitate administrative processing of all application papers, computer readable forms and fees filed under this section. Accordingly, all such application papers, computer readable forms and fees filed in the Office should be marked "Box SEQUENCE."

Correspondence relating to the Sequence Rules may also be hand–delivered to the Group. In cases of hand delivery to the Mail Window or to the Group, the floppy disk should be placed in a protective mailer labeled with at least the application number, if available. The labeling requirements of 37 CFR 1.824(h) must also be complied with. The use of staples and clips, if any, should be confined to carefully attaching the mailer to the submitted papers without contact or compression of the magnetic media which may cause the disk to be unreadable. In no situations,

should additional or complimentary copies of diskettes be delivered to Examiners or other Office personnel.

2423 Symbols and Format To Be Used for Nucleotide and/or Amino Acid Sequence Data

37 CFR 1.822 Symbols and format to be used for nucleotide and/or amino acid sequence data.

(a) The symbols and format to be used for nucleotide and/or amino acid sequence data shall conform to the requirements of paragraphs (b) through (p) of this section.

(b) The code for representing the nucleotide and/or amino acid sequence characters shall conform to the code set forth in the tables in paragraphs (b)(1) and (b)(2) of this section. No code other than that specified in this section shall be used in nucleotide and amino acid sequences. A modified base or amino acid may be presented in a given sequence as the corresponding unmodified base or amino acid if the modified base or amino acid is one of those listed in paragraphs (p)(1) or (p)(2) of this section and the modification is also set forth elsewhere in the Sequence Listing (for example, FEATURES §1.823(b)(2)(ix)). Otherwise, all bases or amino acids not appearing in paragraphs (b)(1) or (b)(2) of this section shall be listed in a given sequence as "N" or "Xaa," respectively, with further information, as appropriate, given elsewhere in the Sequence Listing.

(1) Base codes:

Symbol	Meaning
A	A; adenine
C	C; cytosine
G	G; guanine
T	T; thymine
U	U; uracil
M	A or C
R	A or G
W	A or T/U
S	C or G
Y	C or T/U
K	G or T/U
V	A or C or G; not T/U
H	A or C or T/U; not G
D	A or G or T/U; not C
B	C or G or T/U; not A
N	(A or C or G or T/U) or (unknown or other)

(2) Amino acid three-letter abbreviations:

Abbreviation	Amino acid name
Ala	Alanine
Arg	Arginine
Asn	Asparagine
Asp	Aspartic Acid
Asx	Aspartic Acid or Asparagine
Cys	Cysteine
Glu	Glutamic Acid
Gln	Glutamine
Glx	Glutamine or Glutamic Acid
Gly	Glycine
His	Histidine
Ile	Isoleucine
Leu	Leucine
Lys	Lysine
Met	Methionine
Phe	Phenylalanine
Pro	Proline
Ser	Serine
Thr	Threonine
Trp	Tryptophan
Tyr	Tyrosine
Val	Valine
Xaa	Unknown or other

(c) A nucleotide sequence shall be listed using the one-letter code for the nucleotide bases, as in paragraph (b)(1) of this section.

(d) The amino acids corresponding to the codons in the coding parts of a nucleotide sequence shall be typed immediately below the corresponding codons. Where a codon spans an intron, the amino acid symbol shall be typed below the portion of the codon containing two nucleotides.

(e) The amino acids in a protein or peptide sequence shall be listed using the three-letter abbreviation with the first letter as an upper case character, as in paragraph (b)(2) of this section.

(f) The bases in a nucleotide sequence (including introns) shall be listed in groups of 10 bases except in the coding parts of a sequence. Leftover bases, fewer than 10 in number, at the end of noncoding parts of a sequence shall be grouped together and separated from adjacent groups of 10 or 3 bases by a space.

(g) The bases in the coding parts of a nucleotide sequence shall be listed as triplets (codons).

(h) A protein or peptide sequence shall be listed with a maximum of 16 amino acids per line, with a space provided between each amino acid.

(i) A nucleotide sequence shall be listed with a maximum of 16 codons or 60 bases per line, with a space provided between each codon or group of 10 bases.

(j) A nucleotide sequence shall be presented, only by a single strand, in the 5' to 3' direction, from left to right.

(k) An amino acid sequence shall be presented in the amino to carboxy direction, from left to right, and the amino and carboxy groups shall not be presented in the sequence.

(l) The enumeration of nucleotide bases shall start at the first base of the sequence with number 1. The enumeration shall be continuous through the whole sequence in the direction 5' to 3'. The enumeration shall be marked in the right margin, next to the line containing the one-letter codes for the bases, and giving the number of the last base of that line.

(m) The enumeration of amino acids may start at the first amino acid of the first mature protein, with number 1. The amino acids preceding the mature protein, e.g., pre-sequences, pro-sequences, pre-pro-sequences and signal sequences, when presented, shall have negative numbers, counting backwards starting with the amino acid next to number 1. Otherwise, the enumeration of amino acids shall start at the first amino acid at the amino terminal as number 1. It shall be marked below the sequence every 5 amino acids.

(n) For those nucleotide sequences that are circular in configuration, the enumeration method set forth in paragraph (l) of this section remains

applicable with the exception that the designation of the first base of the nucleotide sequence may be made at the option of the applicant. The enumeration method for amino acid sequences that is set forth in paragraph (m) of this section remains applicable for amino acid sequences that are circular in configuration.

(o) A sequence with a gap or gaps shall be presented as a plurality of separate sequences, with separate sequence identifiers, with the number of separate sequences being equal in number to the number of continuous strings of sequence data. A sequence that is made up of one or more noncontiguous segments of a larger sequence or segments from different sequences shall be presented as a separate sequence.

(p) The code for representing modified nucleotide bases and modified and unusual amino acids shall conform to the code set forth in the tables in paragraphs (p)(1) and (p)(2) of this section. The modified base controlled vocabulary in paragraph (p)(1) of this section and the modified and unusual amino acids in paragraph (p)(2) of this section shall not be used in the nucleotide and/or amino acid sequences; but may be used in the description and/or the "Sequence Listing" corresponding to, but not including, the nucleotide and/or amino acid sequence.

(1) Modified base controlled vocabulary:

Abbreviation	Modified base description
ac4c	4-acetylcytidine
chm5u	5-(carboxyhydroxylmethyl)uridine
cm	2'-O-methylcytidine
cmnm5s2u	5-carboxymethylaminomethyl-2-thioridine
cmnm5u	5-carboxymethylaminomethyluridine
d	dihydrouridine
fm	2'-O-methylpseudouridine
gal q	beta,D-galactosylqueosine
gm	2'-O-methylguanosine
i	inosine
i6a	N6-isopentenyladenosine
m1a	1-methyladenosine
m1f	1-methylpseudouridine
m1g	1-methylguanosine
m1i	1-methylinosine
m22g	2,2-dimethylguanosine
m2a	2-methyladenosine
m2g	2-methylguanosine
m3c	3-methylcytidine
m5c	5-methylcytidine
m6a	N6-methyladenosine
m7g	7-methylguanosine
mam5u	5-methylaminomethyluridine
mam5s2u	5-methoxyaminomethyl-2-thiouridine
man q	beta,D-mannosylqueosine
mcm5s2u	5-methoxycarbonylmethyl-2-thiouridine
mcm5u	5-methoxycarbonylmethyluridine
mo5u	5-methoxyuridine
ms2i6a	2-methylthio-N6-isopentenyladenosine
ms2t6a	N-((9-beta-D-ribofuranosyl-2-methylthiopurine-6-yl) carbamoyl)threonine
mt6a	N-((9-beta-D-ribofuranosylpurine-6-yl)N-methyl-carbamoyl)threonine
mv	uridine-5-oxyacetic acid methylester
o5u	uridine-5-oxyacetic acid (v)
osyw	wybutoxosine
p	pseudouridine
q	queosine
s2c	2-thiocytidine
s2t	5-methyl-2-thiouridine
s2u	2-thiouridine
s4u	4-thiouridine
t	5-methyluridine
t6a	N-((9-beta-D-ribofuranosylpurine-6-yl) carbamoyl) threonine
tm	2'-O-methyl-5-methyluridine
um	2'-O-methyluridine
yw	wybutosine
x	3-(3-amino-3-carboxypropyl)uridine, (acp3)u

(2) Modified and unusual amino acids:

Abbreviation	Modified and unusual amino acid
Aad	2-Aminoadipic acid
bAad	3-aminoadipic acid
bAla	beta-Alanine,beta-Amino-propionic acid
Abu	2-Aminobutyric acid
4Abu	4-Aminobutyric acid, piperidinic acid
Acp	6-Aminocaproic acid
Ahe	2-Aminoheptanoic acid
Aib	2-Aminoisobutyric acid
bAib	3-Aminoisobutyric acid
Apm	2-Aminopimelic acid
Dbu	2,4-Diaminobutyric acid
Des	Desmosine
Dpm	2,2'-Diaminopimelic acid
Dpr	2,3-Diaminopropionic acid
EtGly	N-Ethylglycine
EtAsn	N-Ethylasparagine
Hyl	Hydroxylysine
aHyl	allo-Hydroxylysine
3Hyp	3-Hydroxyproline
4Hyp	4-Hydroxyproline
Ide	Isodesmosine
aIle	allo-Isoleucine
MeGly	N-Methylglycine, sarcosine
MeIle	N-Methylisoleucine
MeLys	6-N-Methyllysine
MeVal	N-Methylvaline
Nva	Norvaline
Nle	Norleucine
Orn	Ornithine

2423.01 Format and Symbols To Be Used in Sequence Listings

37 CFR 1.822 sets forth the format and symbols to be used for listing nucleotide and/or amino acid sequence data. The codes for representing the nucleotide and/or amino acid characters in the sequences are set forth in the tables of 37 CFR 1.822 (b) (1) and37 CFR 1.822 (b) (2). For the purpose of setting forth the sequence in the "Sequence Listing," only those symbols in 37 CFR 1.822(b)(1) for "Base codes" and in 37 CFR 1.822(b) (2) for "Amino acids" are to be used, as further set forth in 37 CFR 1.822 (c) and 37 CFR 1.822(e). No other symbols shall be used in nucleotide and amino acid sequences. The "Modified base controlled vocabulary" in 37 CFR 1.822 (p) (1) and the "Modified and unusual amino acids" in 37 CFR 1.822 (p) (2) are not to be used in setting forth the sequences; but, they may be used in the description and/or the "Sequence Listing" corresponding to, but not including, the sequence itself. A modified base or amino acid may be presented in a given sequence as the corresponding unmodified base or amino acid if the modified base or amino acid is one of those listed in 37 CFR 1.822 (p) (1) or 37 CFR 1.822 (p) (2) and the modification is also set forth elsewhere in the "Sequence Listing;" for example, in the features table. Otherwise, all bases or amino acids not appearing in 37 CFR 1.822 (b) (1) or 37 CFR 1.822 (b) (2) must be listed in a given sequence as "N" or "Xaa," respectively, with further information given elsewhere in the "Sequence Listing." This further information can generally be provided under the "Feature" information item in 37 CFR 1.823(b)(2)(ix).

In 37 CFR 1.822(b)(2) and 37 CFR 1.822(e), the use of three–letter codes for amino acids is required. The use of the three–letter codes for amino acids is preferred over the one–letter codes from the perspective of facilitating the examiner's review of the application papers, including the"Sequence Listing", and the public's, as well as the examiner's, use of the printed patents. The three–letter codes can be presented using the upper case for the first character and lower case for the remaining two characters or all upper case characters. The PatentIn program has the capability of converting from one–letter to three–letter amino acid codes and printing the amino acid sequence in three–letter codes regardless of input.

37 CFR 1.822(d) through (p) set forth the format for presenting sequence data. These paragraphs set forth the manner in which the characters in sequences are to be grouped, spaced, presented and numbered.

2423.02 Depiction of Coding Regions

37 CFR 1.822 (d) requires, in the event that an applicant chooses to depict coding regions, the depiction of amino acids corresponding to codons in the coding parts of a nucleotide sequence immediately below the corresponding codons. Further, in 37 CFR 1.822 (d), the situation in which a codon spans an intron has been addressed. In those situations, the "amino acid symbol shall be typed below the portion of the codon containing two nucleotides." This requirement clarifies the representation of an amino acid that corresponds to a codon that spans an intron.

It should be noted that the sequence rules do not, in any way, require the depiction of coding regions or the amino acids corresponding to the codons in those coding regions. 37 CFR 1.822 (d) only requires that where amino acids corresponding to the codons in the coding parts of a nucleotide sequence are depicted, they must be depicted below the corresponding codons. There is absolutely no requirement in the rules to depict coding regions. Nor is there a requirement to separately list the amino acids corresponding to the codons in the coding parts of a nucleotide sequence unless the applicant desires to discuss the amino acids as a separate sequence. That is, when the coding parts of a nucleotide sequence and their corresponding amino acids have been identified, if applicant desires to discuss those amino acids in the coding parts of the nucleotide as a separate sequence, those amino acids must also be set forth as a separate sequence. The separate submission of the amino acid sequence that corresponds to the coding parts of a nucleotide sequence is, however, recommended and encouraged because the amino acid sequence may not be captured in the sequence database if it is only presented in the "Sequence Listing" as a mixed nucleotide and amino acid sequence.

2423.03 Presentation and Enumeration of Sequences

37 CFR 1.822(j) provides that nucleotide sequences shall only be represented by a single strand, in the 5' to 3'

direction, from left to right. That is, double stranded nucleotides shall not be represented in the "Sequence Listing." A double stranded nucleotide may be represented as two single stranded nucleotides, and any relationship between the two may be shown in the drawings.

The procedures for presenting and numbering amino acid sequences are set forth in 37 CFR 1.822(k) and 37 CFR 1.822 (m). Two alternatives are presented for numbering amino acid sequences. Amino acid sequences may be numbered with respect to the identification of the first amino acid of the first mature protein or with respect to the first amino acid appearing at the amino terminal. The enumeration procedure for nucleotides is set forth in 37 CFR 1.822 (i). Sequences that are circular in configuration are intended to be encompassed by these rules, and numbering procedures for them are provided in 37 CFR 1.822 (n). The numbering procedures set forth in 37 CFR 1.822 (k) through (n) are not necessarily intended to be consistent with all currently employed numbering procedures. The objective here is to establish a reasonable numbering procedure that can readily be followed and adhered to. These formatting procedures also reflect those that have been agreed to for electronic data exchange with the JPO and the EPO.

In 37 CFR 1.822 (o) the procedures for presenting and numbering hybrid and gapped sequences are set forth. A sequence that is made up of one or more noncontiguous segments of a larger sequence or segments from different sequences, i.e., a hybrid sequence, shall be presented as a separate sequence. A "gap" for the purpose of this section is not intended to embrace a gap or gaps that is/are introduced into the presentation of otherwise continuous sequence information in, e.g., a drawing figure, to show alignments or similarities with other sequences. The "gaps" referred to in this section are gaps representing unknown or undisclosed regions in a sequence between regions that are known or disclosed. In the situation where a contiguous fragment of a sequence that has already been properly set forth in a "Sequence Listing" is discussed and/or claimed, the fragment does not need to be separately included in the "Sequence Listing." It may be referred to in the specification, claims or drawings as, e.g., "residues 2 through 33 of SEQ ID NO:12," assuming that SEQ ID NO:12 has been properly included in the "Sequence Listing."

2424 Requirements for Nucleotide and/or Amino Acid Sequences as Part of the Application Papers

37 CFR 1.823. Requirements for nucleotide and/or amino acid sequences as part of the application papers.

(a) The "Sequence Listing," required by § 1.821(c), setting forth the nucleotide and/or amino acid sequences, and associated information in accordance with paragraph (b) of this section, must begin on a new page and be titled "Sequence Listing" and appear immediately prior to the claims. Each page of the "Sequence Listing" shall contain no more than 66 lines and each line shall contain no more than 72 characters. A fixed–width font shall be used exclusively throughout the "Sequence Listing."

(b) The "Sequence Listing" shall, except as otherwise indicated, include, in addition to and immediately preceding the actual nucleotide and/or amino acid sequence, the following items of information. The order and presentation of the items of information in the "Sequence Listing" shall conform to the arrangement given below, except that parenthetical explanatory information following the headings (identifiers) is to be omitted. Each item of information shall begin on a new line, enumerated with the number/numeral/letter in parentheses as shown below, with the heading (identifier) in upper case characters, followed by a colon, and then followed by the information provided. Except as allowed below, no item of information shall occupy more than one line. Those items of information that are applicable for all sequences shall only be set forth once in the "Sequence Listing." The submission of those items of information designated with an "M" is mandatory. The submission of those items of information designated with an "R" is recommended, but not required. The submission of those items of information designated with an "O" is optional. Those items designated with "rep" may have multiple responses and, as such, the item may be repeated in the "Sequence Listing."

(1) GENERAL INFORMATION (Application, diskette/tape and publication information):

(i) APPLICANT (maximum of first ten named applicants; specify one name per line: SURNAME comma OTHER NAMES and/or INITIALS – M/rep):

(ii) TITLE OF INVENTION (title of the invention, as elsewhere in application, four lines maximum – M):

(iii) NUMBER OF SEQUENCES (number of sequences in the "Sequence Listing" – M):

(iv) CORRESPONDENCE ADDRESS (M):

(A) ADDRESSEE (name of applicant, firm, company or institution, as may be appropriate):

(B) STREET (correspondence street address, as elsewhere in application, four lines maximum):

(C) CITY (correspondence city address, as elsewhere in application):

(D) STATE (correspondence state, as elsewhere in application):

(E) COUNTRY (correspondence country, as elsewhere in application):

(F) ZIP (correspondence zip or postal code, as elsewhere in application):

(v) COMPUTER READABLE FORM (M):

(A) MEDIUM TYPE (type of diskette/tape submitted):
(B) COMPUTER (type of computer used with diskette/tape submitted):
(C) OPERATING SYSTEM (type of operating system used):
(D) SOFTWARE (type of software used to create computer readable form):

(vi) CURRENT APPLICATION DATA (M, if available):
(A) APPLICATION NUMBER (U.S application number, including a series code, a slash and a serial number, or U.S. PCT application number, including the letters PCT, a slash, a two letter code indicating the U.S. as the Receiving Office, a two digit indication of the year, a slash and a five digit number, if available):
(B) FILING DATE (U.S. or PCT application filing date, if available; specify as dd–MMM–yyyy):
(C) CLASSIFICATION (IPC/US classification or F–term designation, where F–terms have been developed, if assigned, specify each designation, left justified, within an eighteen position alpha numeric field–rep, to a maximum of ten classification designations):

(vii) PRIOR APPLICATION DATA (prior domestic, foreign priority or international application data, if applicable – M/rep):
(A) APPLICATION NUMBER (application number; specify as two letter country code and an eight digit application number; or if a PCT application, specify as the letters PCT, a slash, a two letter code indicating the Receiving Office, a two digit indication of the year, a slash and a five digit number):
(B) FILING DATE (document filing date, specify as dd–MMM–yyyy):

(viii) ATTORNEY/AGENT INFORMATION (O):
(A) NAME (attorney/agent name; SURNAME comma OTHER NAMES and/or INITIALS):
(B) REGISTRATION NUMBER (attorney/agent registration number):
(C) REFERENCE/DOCKET NUMBER (attorney/agent reference or docket number):

(ix) TELECOMMUNICATION INFORMATION (O):
(A) TELEPHONE (telephone number of applicant or attorney/agent):
(B) TELEFAX (telefax number of applicant or attorney/agent):
(C) TELEX (telex number of applicant or attorney/agent):

(2) INFORMATION FOR SEQ ID NO: X (rep):

(i) SEQUENCE CHARACTERISTICS (M):
(A) LENGTH (sequence length, expressed as number of base pairs or amino acid residues):
(B) TYPE (sequence type, i.e., whether nucleic acid or amino acid):
(C) STRANDEDNESS (if nucleic acid, number of strands of source organism molecule, i.e., whether single stranded, double stranded, both or unknown to applicant):
(D) TOPOLOGY (whether source organism molecule is circular, linear, both or unknown to applicant):

(ii) MOLECULE TYPE (type of molecule sequenced in SEQ ID NO:X (at least one of the following should be included with subheadings, if any, in Sequence Listing – R)):
– Genomic RNA;
– Genomic DNA;
– mRNA
– tRNA;
– rRNA;
– snRNA;
– scRNA;
– preRNA;
– cDNA to genomic RNA;
– cDNA to mRNA;
– cDNA to tRNA;
– cDNA to rRNA;
– cDNA to snRNA;
– cDNA to scRNA;
– Other nucleic acid;
(A) DESCRIPTION (four lines maximum):
– protein and
– peptide.

(iii) HYPOTHETICAL (yes/no – R):
(iv) ANTI–SENSE (yes/no – R):
(v) FRAGMENT TYPE (for proteins and peptides only, at least one of the following should be included in the Sequence Listing – R):
– N–terminal fragment;
– C–terminal fragment and
– internal fragment.

(vi) ORIGINAL SOURCE (original source of molecule sequenced in SEQ ID NO:X – R):
(A) ORGANISM (scientific name of source organism):
(B) STRAIN:
(C) INDIVIDUAL ISOLATE (name/number of individual/isolate):
(D) DEVELOPMENTAL STAGE (give developmental stage of source organism and indicate whether derived from germ–line or rearranged developmental pattern):
(E) HAPLOTYPE:
(F) TISSUE TYPE:
(G) CELL TYPE:
(H) CELL LINE:
(I) ORGANELLE:

(vii) IMMEDIATE SOURCE (immediate experimental source of the sequence in SEQ ID NO:X – R):
(A) LIBRARY (library –type,name):

(B) CLONE (clone(s)):

(viii) POSITION IN GENOME (position of sequence in SEQ ID NO:X in genome – R):

(A) CHROMOSOME/SEGMENT (chromosome/segment – name/number):

(B) MAP POSITION:

(C) UNITS (units for map position, i.e., whether units are genome percent, nucleotide number or other/specify):

(ix) FEATURE (description of points of biological significance in the sequence in SEQ ID NO:X –R/rep):

(A) NAME/KEY (provide appropriate identifier for feature – four lines maximum):

(B) LOCATION (specify location according to syntax of DDBJ/EMBL/GenBank Feature Tables Definition, including whether feature is on complement of presented sequence; where appropriate state number of first and last bases/amino acids in feature – four lines maximum):

(C) IDENTIFICATION METHOD (method by which the feature was identified, i.e., by experiment, by similarity with known sequence or to an established consensus sequence, or by similarity to some other pattern – four lines maximum):

(D) OTHER INFORMATION (include information on phenotype conferred, biological activity of sequence or its product, macromolecules which bind to sequence or its product, or other relevant information – four lines maximum):

(x) PUBLICATION INFORMATION (Repeat section for each relevant publication – O/rep):

(A) AUTHORS (maximum of first ten named authors of publication; specify one name per line: SURNAME comma OTHER NAMES and/or INITIALS – rep):

(B) TITLE (title of publication):

(C) JOURNAL (journal name in which data published):

(D) VOLUME (journal volume in which data published):

(E) ISSUE (journal issue number in which data published):

(F) PAGES (journal page numbers in which data published):

(G) DATE (journal date in which data published; specify as dd–MMM–yyyy, MMM–yyyy or Season–yyyy):

(H) DOCUMENT NUMBER (document number, for patent type citations only; specify as two letter country code, eight digit document number (right justified), one letter and, as appropriate, one number or a space as a document type code; or if a PCT application, specify as the letters PCT, a slash, a two letter code indicating the Receiving Office, a two digit indication of the year, a slash and a five digit number; or if a PCT publication, specify as the two letters WO, a two digit indication of the year, a slash and a five digit publication number):

(I) FILING DATE (document filing date, for patent–type citations only; specify as dd–MMM– yyyy):

(J) PUBLICATION DATE (document publication date; for patent–type citations only, specify as dd–MMM–yyyy):

(K) RELEVANT RESIDUES IN SEQ ID NO:X (rep): FROM (position) TO (position)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:X:

2424.01 Informational Requirements for the Sequence Listing

37 CFR 1.823 sets forth the informational requirements for inclusion in the separate part of the disclosure on paper copy (the "Sequence Listing") that must be submitted in accordance with 37 CFR 1.821(c). This section lists the items of information that are to be included in the "Sequence Listing," which constitutes the separate part of the disclosure on paper copy. The items of information are to be presented in the "Sequence Listing," immediately preceding the actual nucleotide and/or amino acid sequence, in the order in which those items are listed in this section. Page and line length requirements are set forth. The requirement to use a fixed width font to present sequence data is also set forth. This latter requirement is made to ensure that the desired sequence character spacing and numbering is maintained upon printing. The heading for each item of information shall not include the parenthetical explanatory information included in this section.

2424.02 Categories of Information Items

In 37 CFR 1.823, the items of information are broken down into two categories. The first category is directed to "GENERAL INFORMATION" and includes information relating to the application being filed and the diskette/tape being submitted. This information will be applicable for all sequences and, as such, will need to be set forth only once in a given "Sequence Listing." The second category is directed to "INFORMATION FOR SEQ ID NO:X" and includes information that will be specific for each sequence disclosed. Where more than one sequence is disclosed, this category will be repeated and subsequent headings should be set forth as: "(2) INFORMATION FOR SEQ ID NO:2:," "(2) INFORMATION FOR SEQ ID NO:3:," etc.

Throughout the above two categories, the items of information are further broken down into categories relating to whether their submission is mandatory (M), recommended (R) or optional (O). Certain items are also designated as those that may repeat (rep) in a given "Sequence Listing." The numbering of repeated items should remain constant so that the overall numbering scheme of the "Sequence Listing" conforms to that specified in this section. The first category includes those items for which inclusion in the "Sequence Listing" is mandatory. These mandatory items of information relate to the patent application, the computer readable form, basic sequence data and the applicable priority or PCT data. The reference in 37 CFR 1.823(b)(1)(vi)(C) to "F-terms" relates to the key-word indexing of patents that is being undertaken by the JPO in conjunction with their automation plans. The second category includes those items for which inclusion in the "Sequence Listing" is recommended, but not required. These recommended items of information provide further information relating to the sequence listed. These additional items of information are of interest to examiners and will create a more comprehensive database; as a result, the items would serve to facilitate sequence searching. The third category includes items of information that are primarily for the purpose of providing more complete information upon dissemination, for which inclusion in the "Sequence Listing" is also optional.

2424.03 Additional Miscellaneous Requirements

Throughout 37 CFR 1.823(b)(1) and 37 CFR 1.823(b)(2), the items of information relating to patent applications and patent publications should be provided keeping in mind the appropriate standards that have been established by the World Intellectual Property Organization (WIPO). In general, an application should be identified by a country code, a number and a filing date, while a published patent document should be identified by a country code, a number and kind code. Proper citation of priority patent applications is covered in MPEP § 201.14(d). For published patent documents, the country code, number and kind code will appear on the front page of the document. Unpublished PCT applications are identified by the letters PCT, the country code of the Receiving Office, the last two digits of the year of filing and a number, e.g., PCT/AT81/00033, PCT/FR88/00100. A published PCT application is identified by the letters WO, the last two digits of the year of publication, a number and a kind code, e.g., WO82/02827A, WO88/06811A. Country codes from WIPO Standard ST.3 are reproduced in MPEP § 1870 Annex B and kind codes from WIPO Standard ST.16 are reproduced in MPEP § 1871 as Appendix II. Questions on proper citation of patent documents should be directed to the Search and Information Resources Administration, International Liaison Staff.

In 37 CFR 1.823(b)(1)(i), the item of information relating to "APPLICANT" should be limited to a maximum of the first ten named applicants in the application. Similarly, in 37 CFR 1.823(b)(2)(x), the item of information relating to "AUTHORS" should be limited to to a maximum of the first ten named authors in the publication.

In 37 CFR 1.823(b)(1)(v)(B), 37 CFR 1.823(b)(1)(vi)(C) and 37 CFR 1.823(b)(1)(vi)(D), "dd-MMM-yyyy" is the format for the presentation of date information in the "Sequence Listing." The lower case letters designate numeric responses and the upper case letters designate alphabetical responses. As such, March 2, 1988, would be presented as 02-MAR-1988. In 37 CFR 1.823(b)(2)(x)(G), "dd-MMM-yyyy, MMM-yyyy or Season-yyyy" encompass all variations in date designations that may be encountered.

In 37 CFR 1.823(b)(2)(ix), relating to "FEATURES" or the description of the points of biological significance in a given sequence, it is recommended, but not required, that the information that is provided by the applicant conform to the controlled vocabulary that is set forth in GenBank's "Feature Representation in Nucleotide Sequence Data Libraries," Release 57.0, as may be amended. Further, the feature "LOCATION" should be specified using the syntax of the DDBJ/EMBL/GenBank Feature Table Definition.

In 37 CFR 1.823(b)(2)(x), publication information for a given sequence is collected. The publication information encompasses both patent-type publications and non-patent literature publications. Information item "(K) RELEVANT RESIDUES IN SEQ ID NO: X" is intended to collect information relating to the correspondence between a sequence set forth in the "Sequence Listing" and published sequence information. The starting (FROM) and end (TO) positions in the listed sequence that correspond to the published sequence information should be set forth.

2425 Form and Format for Nucleotide and/or Amino Acid Sequence Submissions in Computer Readable Form

37 CFR 1.824 Form and format for nucleotide and/or amino acid sequence submissions in computer readable form.

(a) The computer readable form required by § 1.821(e) shall contain a printable copy of the "Sequence Listing," as defined in §§ 1.821(c), 1.822 and 1.823, recorded as a single file on either a diskette or a magnetic tape. The computer readable form shall be encoded and formatted such that a printed copy of the "Sequence Listing" may be recreated using the print commands of the computer/operating–system configurations specified in paragraph (f) of this section.

(b) The file in paragraph (a) of this section shall be encoded in a subset of the American Standard Code for Information Interchange (ASCII). This subset shall consist of all the printable ASCII characters including the ASCII space character plus line–termination, pagination and end–of–file characters associated with the computer/operating–system configurations specified in paragraph (f) of this section. No other characters shall be allowed.

(c) The computer readable form may be created by any means, such as word processors, nucleotide/amino acid sequence editors or other custom computer programs; however, it shall be readable by one of the computer/operating–system configurations specified in paragraph (f) of this section, and shall conform to the specifications in paragraphs (a) and (b) of this section.

(d) The entire printable copy of the "Sequence Listing" shall be contained within one file on a single diskette or magnetic tape unless it is shown to the satisfaction of the Commissioner that it is not practical or possible to submit the entire printable copy of the "Sequence Listing" within one file on a single diskette or magnetic tape.

(e) The submitted diskette or tape shall be write–protected such as by covering or uncovering diskette holes, removing diskette write tabs or removing tape write rings.

(f) As set forth in paragraph (c), above, any means may be used to create the computer readable form, as long as the following conditions are satisfied. A submitted diskette shall be readable on one of the computer/operating–system configurations described in paragraphs (1) through (3), below. A submitted tape shall satisfy the format specifications described in paragraph (4), below.

(1) Computer: IBM PC/XT/AT, IBM PS/2 or compatibles;
Operating system: PC–DOS or MS–DOS (Versions 2.1 or above);
Line Terminator: ASCII Carriage Return plus ASCII Line Feed;
Pagination: ASCII Form Feed or Series of Line Terminators;
End–of–File: ASCII SUB (Ctrl–Z);
Media: Diskette – 5.25 inch, 360 Kb storage;
Diskette – 5.25 inch, 1.2 Mb storage;
Diskette – 3.50 inch, 720 Kb storage;
Diskette – 3.50 inch, 1.44 Mb storage;
Print Command: PRINT filename.extension;

(2) Computer: IBM PC/XT/AT, IBM PS/2 or compatibles;
Operating system: Xenix;
Line Terminator: ASCII Carriage Return;
Pagination: ASCII Form Feed or Series of Line Terminators;
End–of–File: None;
Media: Diskette – 5.25 inch, 360 Kb storage;
Diskette – 5.25 inch, 1.2 Mb storage;
Diskette – 3.50 inch, 720 Kb storage;
Diskette – 3.50 inch, 1.44 Mb storage;
Print Command: lpr filename;

(3) Computer: Apple Macintosh;
Operating System: Macintosh;
Macintosh File Type: text with line termination
Line Terminator: Pre–defined by text type file;
Pagination: Pre–defined by text type file;
End–of–file: Pre–defined by text type file;
Media: Diskette – 3.50 inch, 400 Kb storage;
Diskette – 3.50 inch, 800 Kb storage;
Diskette – 3.50 inch, 1.4 Mb storage;
Print Command: Use PRINT command from any Macintosh Application that processes text files, such as MacWrite or TeachText;

(4) Magnetic tape: 0.5 inch, up to 2400 feet;
Density: 1600 or 6250 bits per inch, 9 track;
Format: raw, unblocked;
Line Terminator: ASCII Carriage Return plus optional ASCII Line Feed;
Pagination: ASCII Form Feed or Series of Line Terminators;
Print Command (Unix shell version given here as sample response – mt/dev/rmt0; lpr</dev/rmt0):

(g) Computer readable forms that are submitted to the Office will not be returned to the applicant.

(h) All computer readable forms shall have a label permanently affixed thereto on which has been hand printed or typed, a description of the format of the computer readable form as well as the name of the applicant, the title of the invention, the date on which the data were recorded on the computer readable form and the name and type of computer and operating system which generated the files on the computer readable form. If all of this information can not be printed on a label affixed to the computer readable form, by reason of size or otherwise, the label shall include the name of the applicant and the title of the invention and a reference number, and the additional information may be provided on a container for the computer readable form with the name of the applicant, the title of the invention, the reference number and the additional information affixed to the container. If the computer readable form is submitted after the date of filing under 35 U.S.C. 111, after the date of entry in the national stage under 35 U.S.C. 371 or after the time of filing, in the United States Receiving Office, an international application under the PCT, the labels mentioned herein must also include the date of the application and the application number, including series code and serial number.

37 CFR 1.824 sets forth the requirements for sequence submissions in computer readable form. Any computer operating system may be utilized to produce a

sequence submission, provided that the system is capable of producing a file having the characteristics specified in 37 CFR 1.824, and is capable of writing the properly formatted file to one of the acceptable diskettes or tapes. Currently, the computer readable form is limited to diskettes or tapes. However, as noted above, it is contemplated that this may be broadened in the future in light of progress in the technology for developing and establishing databases of this type. That is, it is possible that this may be broadened in the future to encompass other media and formats. If a given sequence and its associated information cannot practically or possibly fit on a single diskette or tape, as is required in 37 CFR 1.824(d), an exception via a non–fee petition to waive this provision will normally be granted. As set forth in 37 CFR 1.824(g), the computer readable forms that are submitted in accordance with these rules will not be returned to the applicant. 37 CFR 1.824(h) requires the labeling, with appropriate identifying information, of the computer readable forms that are submitted in accordance with these rules.

2426 Amendments to or Replacement of Sequence Listing and Computer Readable Copy Thereof

37 CFR 1.825 Amendments to or replacement of sequence listing and computer readable copy thereof.

(a) Any amendment to the paper copy of the "Sequence Listing" (§ 1.821(c)) must be made by the submission of substitute sheets. Amendments must be accompanied by a statement that indicates support for the amendment in the application, as filed, and a statement that the substitute sheets include no new matter. Such a statement must be a verified statement if made by a person not registered to practice before the Office.

(b) Any amendment to the paper copy of the "Sequence Listing," in accordance with paragraph (a) of this section, must be accompanied by a substitute copy of the computer readable form (§ 1.821(e)) including all previously submitted data with the amendment incorporated therein, accompanied by a statement that the copy in computer readable form is the same as the substitute copy of the "Sequence Listing." Such a statement must be a verified statement if made by a person not registered to practice before the Office.

(c) Any appropriate amendments to the "Sequence Listing" in a patent, e.g., by reason of reissue or certificate of correction, must comply with the requirements of paragraphs (a) and (b) of this section.

(d) If, upon receipt, the computer readable form is found to be damaged or unreadable,

applicant must provide, within such time as set by the Commissioner, a substitute copy of the data in computer readable form accompanied by a statement that the substitute data is identical to that originally filed. Such a statement must be a verified statement if made by a person not registered to practice before the Office.

37 CFR 1.825 sets forth the procedures for amending the "Sequence Listing" and the computer readable copy thereof. The procedures that have been defined in this section involve the submission of either substitute sheets of the "Sequence Listing" or substitute copies of the computer readable form, in conjunction with statements that indicate support for the amendment in the application, as filed, and that the substitute sheets or copies include no new matter. (See MPEP § 2428 for further information and Sample Statements.) The requirement for statements regarding the absence of new matter follows current practice relating to the submission of substitute specifications, as set forth in 37 CFR 1.125. 37 CFR 1.825 (c) addresses the situation where amendments to the "Sequence Listing" are made after a patent has been granted, e.g., by a certificate of correction, reissue or reexamination. 37 CFR 1.825 (d) addresses the possibility and presents a remedy for the situation where the computer readable form may be found by the Office to be damaged or unreadable.

2427 Form Paragraphs and Notice to Comply

2427.01 Form Paragraphs

In order to minimize the extension of pendency due to the implementation of the sequence rules, all compliance issues should be addressed in a single communication with the applicant. That communication should set a 1–month period for response that may be extended in accordance with the provisions of 37 CFR 1.136. However, depending upon the nature of applicant's response, a followup communication regarding the sequence rules may be necessary. The form paragraphs that follow are to be used in these communications. The form paragraphs should be used as follows:

7.200 – This form paragraph should be used for the first mailing of a Notice to Comply.

7.201 – This form paragraph should be used for the first mailing of a CRF Diskette Problem Report.

7.202 – This form paragraph should be used when an applicant has made a bona fide attempt to comply but the response generates an error listing from the Scientific and Technical Information Center (STIC). This should be used for a second mailing to applicant unless it is evident that there has been a deliberate omission; this form paragraph may also be used to extend the period for response for the initially mailed notice.

7.203 – This form paragraph should be used when there has been a deliberate omission in the response or where the reason the response is incomplete cannot be characterized as an apparent oversight or instance of inadvertence.

¶ *7.200 Cover Letter for Use with Notice to Comply with Sequence Rules*

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Any inquiry concerning this communication should be directed to Examiner [1], Art Unit [2], whose telephone number is (703) 308–[3]. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

APPLICANT IS GIVEN ONE MONTH FROM THE DATE OF THIS LETTER WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 CFR 1.821 – 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136. In no case may an applicant extend the period for response beyond the six month statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Examiner notes:

1. Use this form paragraph **only for the initial communication to the applicant.** Use either 7.202 or 7.203 for subsequent communications.

2. Insert appropriate information in brackets.

3. Print this paragraph on a PTOL–90 and attach a Notice to Comply With Requirements for Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures, along with a marked–up copy of the Raw Sequence Listing, if any. If the PTOL–90 has a pre–printed response period heading, it should be blocked out.

¶ *7.201 Cover Letter for Use with CRF Diskette Problem Report*

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). A computer readable form (CRF) of the sequence listing was submitted. However, the CRF could not be processed by the Scientific and Technical Information Center (STIC) for the reason(s) set forth on the attached CRF Diskette Problem Report.

Any inquiry concerning this communication should be directed to Examiner [1], Art Unit [2], whose telephone number is (703) 308–[3].

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

APPLICANT IS GIVEN ONE MONTH FROM THE DATE OF THIS LETTER WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 CFR 1.821 – 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136. In no case may an applicant extend the period for response beyond the six month statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached CRF Diskette Problem Report with the response.

Examiner notes:

1. Use this form paragraph **only for the initial communication to the applicant.** Use either 7.202 or 7.203 for subsequent communications.

2. Insert appropriate information in brackets.

3. Print this paragraph on a PTOL–90 and attach the CRF Diskette Problem Report. If the PTOL–90 has a preprinted response period heading, it should be blocked out.

¶ *7.202 CRF Submission Is Not Fully Responsive, Bona Fide Attempt*

The communication filed on [1] is not fully responsive to the communication mailed [2] for the reason(s) set forth on the attached Notice to Comply With the Sequence Rules or CRF Diskette Problem Report.

Since the response appears to be **bona fide**, but through an apparent oversight or inadvertence failed to provide a complete response, applicant is required to complete the response within a time limit of one (1) month from the date of this letter or within the time remaining in the response period of the communication mailed [3], whichever is the longer. 37 CFR 1.135(c).

NO EXTENSION OF THIS TIME LIMIT MAY BE GRANTED UNDER EITHER 37 C.F.R. 1.136(a) OR (b), BUT THE STATUTORY PERIOD FOR RESPONSE SET IN THE COMMUNICATION MAILED [4] MAY BE EXTENDED UP TO A MAXIMUM OF SIX (6) MONTHS UNDER 37 CFR 1.136.

Examiner notes:

1. This form paragraph may be used whether or not the six–month period for response has expired.

It is intended for use whenever a **bona fide** response has been submitted. This practice does not apply where there has been a deliberate omission of some necessary part of a complete response or where the reason the response is incomplete cannot be characterized as an apparent oversight or apparent inadvertence. Under such cases the examiner has no authority to grant an extension if the six–month period for response has expired. Use form paragraph 7.203 under such circumstances.

2. In bracket 1 insert the date of the response and in brackets 2, 3 and 4 insert the mail date of the communication requiring compliance.

3. Print this paragraph on a PTOL–90 and attach a Notice to Comply With Requirements for Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures, along with a marked–up copy of the Raw Sequence Listing, or CRF Diskette Problem Report. If the PTOL–90 has a pre–printed response period heading, it should be blocked out.

4. See 37 CFR 1.135(c), 1.821(g); MPEP 710.02(c), 711.02(a), 714.02, 714.03.

¶ *7.203 CRF Submission Is Not Fully Responsive*

The communication filed on [1] is not fully responsive to the communication mailed [2] for the reason(s) set forth on the attached

Notice to Comply With the Sequence Rules or CRF Diskette Problem Report.

If a complete response has not been submitted by the time the shortened statutory period for response set in the communication mailed [3] has expired, this application will become abandoned unless applicant corrects the deficiency and obtains an extension of time under 37 C.F.R. 1.136. In no case may an applicant extend the period for response beyond the six month statutory period.

Examiner notes:

1. This form paragraph **may not** be used when the six–month period for response has expired. Use this form paragraph in the situation where in the response (within the six–months) there has been a deliberate omission of some necessary part of a complete response. When the response appears to be **bona fide**, but through an apparent oversight or inadvertence failed to provide a complete response, use form paragraph 7.202.

2. In bracket 1 insert the date of the response and in brackets 2 and 3 insert the mail date of the communication requiring compliance.

3. Print this paragraph on a PTOL–90 and attach a Notice to Comply With Requirements for Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures, along with a marked–up copy of the Raw Sequence Listing, or CRF Diskette Problem Report. If the PTOL–90 has a pre–printed response period heading, it should be blocked out.

2427.02 Notice To Comply

The text of the Notice to Comply with the requirements of the sequence rules follows. The appropriate box on the notice should be checked depending upon the particular deficiencies that have been identified. A copy of the "Raw Sequence Listing," where available, should also be sent to the applicant. The "Raw Sequence Listing" should also be entered into the application file upon receipt from STIC.

Application No. _____

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 CFR 1.821 –1.825 for the following reason(s):

1. This application clearly fails to comply with the requirements of 37 CFR 1.821 –1.825. Applicant's attention is directed to these regulations, published at 1114 O.G. 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 CFR 1.821(c).

3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 CFR 1.821(e).

4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 CFR 1.822 and/or 1.823, as indicated on the attached copy of the marked–up "Raw Sequence Listing."

5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A substitute computer readable form must be submitted as required by 37 CFR 1.825(d).

6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 CFR 1.821(e).

7. Other:_____

Applicant must provide:

_ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing"

_ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification

_ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 CFR 1.821(e) or 37 CFR 1.821(f) or 37 CFR 1.821(g) or 37 CFR 1.825(b) or 37 CFR 1.825(d).

For questions regarding compliance with these requirements, please contact:

For Rules Interpretation, call (703) 308–1123
For CRF submission help, call (703) 308–4212
For PatentIn software help, call (703) 557–0400

Please return a copy of this notice with your response.

2428 Sample Statements

Sample language for the statements required to support sequence rule submissions is provided below. These statements are given by way of example only, other language may, of course, be used. For the statements that relate to the assertion that the content of the paper and computer readable copies are the "same," it is acknowledged that there may be some non–substantive differences between the two, e.g., page numbers and page breaks may be present in the paper copy but not in the computer readable copy thereof. This requirement for sameness relates to the informational content of the paper and computer readable copies relevant to the requirements of the sequence rules.

37 CFR 1.821(f) – I hereby state that the content of the paper and computer readable copies of the Sequence Listing, submitted in accordance with 37 CFR 1.821(c) and (e), respectively, are the same.

37 CFR 1.821(g) [or (h)] – I hereby state that the submission, filed in accordance with 37 CFR 1.821(g) [or (h)], herein does not include new matter [or go beyond the disclosure in the international application].

37 CFR 1.825(a) – I hereby state that the amendments, made in accordance with 37 CFR 1.825(a), included in the substitute sheet(s) of the Sequence Listing are supported in the application, as filed, at _____. I hereby state that the substitute sheet(s) of the Sequence Listing does (do) not include new matter.

37 CFR 1.825(b) – I hereby state that the substitute copy of the computer readable form, submitted in accordance with 37 CFR 1.825(b), is the same as the amended Sequence Listing.

37 CFR 1.825(d) – I hereby state that the substitute copy of the computer readable form, submitted in accordance with 37 CFR 1.825(d), is identical to that originally filed.

A sample verification, see also 37 CFR 1.68, follows:

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

2429 Helpful Hints for Compliance

The Office has now had a good deal of experience in the implementation of the sequence rules. The following list sets forth helpful hints, for both examiners and applicants, for compliance. For the most part, the list is a compilation of frequently asked questions.

— Compliance is not a filing date issue.

— Compliance is not a 35 U.S.C. 112 issue.

— Compliance is not a 35 U.S.C. 119/120 issue.

— Compliance is not a new matter issue. The standard for resolution of inconsistencies between the paper and the electronic copies and/or errors in the paper copy of sequence information is based on the new matter standard.

— Compliance can be achieved via amendment.

— The paper copy of Sequence Listing is an integral part of the application. The Sequence Listing should begin on a new page immediately prior to the claims, with pages numbered consecutively with the rest of the application. The new page that begins the "Sequence Listing" should be entitled "Sequence Listing." If not submitted as such at filing, the Sequence Listing must be inserted into the application via amendment, e.g., by preliminary amendment.

— Substitute pages must be used for changes to the Sequence Listing.

— Punctuation, information item headings and parentheses listed in 37 CFR 1.823 are very important for our database. Extra colons and parentheses should not be used in Sequence Listings.

— The computer readable form cannot contain page numbers. Page numbers should only be placed on the paper copy of the Sequence Listing.

— The PatentIn computer program is not the only means by which to comply with the rules. Any word processing program can be used to generate a Sequence Listing if it has the capability to convert a file into ASCII text.

— If a word processing program is used to generate a "Sequence Listing," hard page break controls should not be used and margins should be adjusted to the smallest setting.

— However, word processing files should not be submitted to the Office; the Sequence Listing generated by a word processing file should be saved as an ASCII text file for submission. Most word processing programs provide this feature.

— Statements in accordance with 37 CFR 1.821(f), (g), (h) and 37 CFR 1.825 and proper labeling in accordance with 37 CFR 1.824(h) should be noted. Sample statements to support filings and submissions in accordance with 37 CFR 1.821 through 1.825 are provided in MPEP § 2428 Sample Statements.

— Use Box Sequence – 37 CFR 1.821(j).

— Three and a half inch disks are less fragile than five and a quarter inch disks.

— On nucleotide sequences, since only single strands may be depicted in the "Sequence Listing," please remember to show strands in 5' to 3' direction.

— The single stranded nucleotide depicted in the "Sequence Listing" may represent a strand of a nucleotide sequence that may be single or double stranded which may be, further, linear or circular. An amino acid sequence or peptide may be linear or circular. In some instances, a sequence may be both single stranded and double stranded and/or both linear and circular. The response "not relevant" is also an acceptable response for both "Strandedness" and "Topology."

— Current Application Data and Prior Application Data fields should always be supplied even if left blank. The Current Application Data headings should appear in the "Sequence Listing" in all cases. If the information about the current application is not known or is unavailable at the time of completing the Sequence Listing, then the line following each heading should be left blank. This would normally be the case when the "Sequence Listing" is included in a newly filed application. Similarly, if information regarding

prior applications is inapplicable or not known at the time of completing the "Sequence Listing" but will be later filed, then the Prior Application Data field headings should appear with the line following the heading left blank.

— Margin requirements and minimum character size for the Sequence Listing must be complied with and can usually be satisfied by using 10 point, 12 pitch type.

— If you receive a Notice to Comply that should not have been sent to you, a simple letter, in the form of a request for reconsideration of the notice, to the organization sending the notice should suffice to clarify the matter.

— There are a limited number of Mandatory Items of Information. They are listed in MPEP § 2433 Sequence Listing Headings for Mandatory Items.

— Figures can be used to convey information not readily conveyed by the Sequence Listing. The exclusive conformance requirement of 37 CFR1.821(b) will be relaxed for drawing figures. However, the sequence information so conveyed must still be included in a "Sequence Listing" and the sequence identifier ("SEQ ID NO:X") must be used, either, in the drawing or in the "Brief Description of the Drawings."

— Extra copies of computer readable forms should not be sent to examiners.

— Inosine should be represented by the use of "N".

— Stop codons, represented by an asterisk, are not permitted in amino acid sequences.

— Punctuation should not be used in a sequence to indicate unknown nucleotide bases or amino acid residues nor should punctuation be used to delimit active or functional regions of a sequence. These regions should be noted as Features of the sequence per 37 CFR 1.823(b)(2)(ix).

— The presence of an unnatural amino acid in a sequence does not have the same effect as the presence of a D−amino acid. The sequence may still be subject to the rules even though one or more of the amino acids is not naturally occurring.

— Cyclic and branched peptides are causing some confusion in the application of the rules. Specific questions should be directed to Group 1800 personnel.

— A cyclic peptide with a tail is regarded as a branched sequence, and thereby exempt from the rules, if all bonds adjacent to the amino acid from which the tail emanates are normal peptide bonds.

— Representations of amino acid sequences, such as $XY(AA)_nZ$ where X, Y and Z can be various amino acids (properly formatted as Xaas) and $(AA)_n$ is a spacer where AA can be any amino acid and n can be 0, 1, 2 or 3, are exempt from the rules. In the specific example given, the sequence is exempt due to the presence of the spacer in which the variable AA, which would properly be represented as Xaa, can be zero, one, two or three amino acids. In general, at a given position in a sequence, that position must be occupied by a single constituent, even though that single constituent might be a variable, such as an Xaa or an N.

— Single letter amino acid abbreviations are not acceptable anywhere in the application, including the "Sequence Listing."

— Zero (0) is not used when the numbering of amino acids uses negative numbers to distinguish the mature protein.

— Subscripts or superscripts are not permitted in "Sequence Listings."

— If a "Sequence Listing" is amended, an entirely new computer readable form is required regardless of the triviality of the amendment. Amendments to the paper copy of the "Sequence Listing" must be made by substitute sheets.

— Note field length limitations. For specific instances, they may be waived, but compliance is encouraged.

— The exclusive conformance requirement of 37 CFR 1.821(b) requires that any amendment of the sequence information in a "Sequence Listing" be accompanied by an amendment to the corresponding information, if any, embedded in the text of the specification or presented in a drawing figure.

— Any inquiries regarding a specific computer readable form that has been processed by the Office should be directed to the Systems Branch of the Biotechnology Division of the Scientific and Technical Information Center.

2430 Patent In Information; Utilities Programs; Training

In those areas of biotechnology in which nucleotide and/or amino acid sequence information is significant, many patent applicants are accustomed to, or familiar with, the submission of such sequence information, in

electronic form, to various sequence databases, such as GenBank, which is produced by the National Institutes of Health. In order to facilitate such submissions, or merely for the purpose of researching and developing sequence information, many eventual patent applicants also generate or encode sequence information in computer readable form. In order to further facilitate compliance with the sequence rules, the Office has made available to the public an input program that is based on the AuthorIn program produced by GenBank. This input program is specifically tailored to the requirements of the sequence rules and will generate both the paper and electronic copies of a Sequence Listing that comply with the requirements of the rules. The input program is called PatentIn. It is available from the Office for $480.00 and can be paid for by check made out to the Commissioner of Patents and Trademarks or by debit to a deposit account. Copies can be obtained by written request to: Commissioner of Patents and Trademarks, Patent and Trademark Office, Washington, D.C. 20231, Attention – Lois E. Boland, Special Program Examiner, Office of the Assistant Commissioner for Patents, Crystal Park 2 – Suite 919. Additional information regarding PatentIn orders can be obtained from the Search and Information Resources Administration, Crystal Park 3 – Suite 702 at (703) 557–0400. Copies can be obtained by facsimile request if the authorization to debit a deposit account is included. Facsimile requests should be directed to: (703) 557–0668 or (703) 305–8825.

PatentIn is available for IBM PC XT, AT, PS/2 and compatible computers. It runs only on a system with a hard disk drive. MS–DOS or PC–DOS Version 3.0 or higher is recommended. Installation of PatentIn on a hard disk requires a minimum of 1.2 megabytes free disk space. The program requires a PC with 550 kilobytes free in RAM (random access memory). A MacIntosh version of PatentIn is not available.

The PatentIn program materials include four program diskettes (3 1/2 or 5 1/4 inch), a PatentIn User Manual, a PatentIn Quick Reference Card, and Supplemental Instructions for the PatentIn Program. The Supplemental Instructions address, among other things, known bugs and operational difficulties, common editing problems, asterisks in peptide sequences and the use of ASCII text editors or word processors. For those purchasing the program, software support is also provided by the Office through the Search and Information Resources Administration.

The Office, in cooperation with the European Patent Office, has developed a group of utilities programs that facilitate sequence manipulation and aid in the conversion of a PatentIn Sequence Listing to a format that complies with the European Patent Office submission rules. Copies of the utilities programs can be obtained through the Search and Information Resources Administration.

While use of the PatentIn program is not required for compliance with the sequence rules, its use is highly recommended as Office experience has shown that submissions developed with PatentIn are far less likely to include errors than those developed without the program The many automatic features of the PatentIn program also greatly ease the generation of Sequence Listings when compared to generating them by hand in a word processing environment. This is especially true for Sequence Listings that include many sequences and/or sequences having great lengths.

The Office provides hands–on training in the use of the PatentIn and associated utilities programs. The classes are held in Washington D.C. as demand warrants. In addition, on site training may be arranged at locations outside Washington, D.C. To express interest in such classes, please contact the Search and Information Resources Administration.

2431 Sample Sequence Listing

A sample "Sequence Listing" is included below. As indicated, it is only necessary to list information that is applicable to a given sequence in the "Sequence Listing." The sample "Sequence Listing" also serves to illustrate that when the coding parts of a nucleotide sequence and their corresponding amino acids have been identified, if applicant desires to discuss those amino acids in the coding parts of the nucleotide as a separate sequence, those amino acids must also be set forth as a separate sequence. In the given sample, it can be assumed that the applicant desired to discuss the amino acids as a separate sequence. This convention will minimize ambiguities that may result in those instances where the amino acids corresponding to the coding parts of a nucleotide sequence constitute two separate amino acid sequences. In those instances, if an applicant desires to discuss the two separate amino acid sequences, they must be separately presented in the "Sequence Listing." Further, in those instances when applicant desires to discuss, as separate sequences, all three reading frames of

the coding regions of a nucleotide sequence, six separate sequences should be set forth in the "Sequence Listing" to minimize confusion. These six sequences, each having a different sequence identifier, would include three nucleotide sequences separately showing each of the three reading frames of the coding regions of the sequence and three separate amino acid sequences corresponding to the translation of the three reading frames of the nucleotide sequence.

SAMPLE SEQUENCE LISTING

(1) GENERAL INFORMATION:
- (i) APPLICANT: Doe, Joan X
  Doe, John Q
- (ii) TITLE OF INVENTION: Isolation and Characterization of a Gene Encoding a Protease from Paramecium sp.
- (iii) NUMBER OF SEQUENCES: 2
- (iv) CORRESPONDENCE ADDRESS:
  - (A) ADDRESSEE: Smith and Jones
  - (B) STREET: 123 Main Street
  - (C) CITY: Smalltown
  - (D) STATE: Anystate
  - (E) COUNTRY: USA
  - (F) ZIP: 12345
- (v) COMPUTER READABLE FORM:
  - (A) MEDIUM TYPE: Diskette, 3.50 inch, 800 Kb storage
  - (B) COMPUTER: Apple Macintosh
  - (C) OPERATING SYSTEM: Macintosh 5.0
  - (D) SOFTWARE: MacWrite
- (vi) CURRENT APPLICATION DATA:
  - (A) APPLICATION NUMBER: 09/999,999
  - (B) FILING DATE: 28-FEB-1989
  - (C) CLASSIFICATION: 999/99
- (vii) PRIOR APPLICATION DATA:
  - (A) APPLICATION NUMBER: PCT/US88/99999
  - (B) FILING DATE: 01-MAR-1988
- (viii) ATTORNEY/AGENT INFORMATION:
  - (A) NAME: Smith, John A
  - (B) REGISTRATION NUMBER: 00001
  - (C) REFERENCE/DOCKET NUMBER: 01-0001
- (ix) TELECOMMUNICATION INFORMATION:
  - (A) TELEPHONE: (909) 999-0001
  - (B) TELEFAX: (909) 999-0002

(2) INFORMATION FOR SEQ ID NO:1:
- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 954 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii)MOLECULE TYPE: genomic DNA
- (iii) HYPOTHETICAL: yes
- (iv) ANTI-SENSE: no
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Paramecium sp
  - (C) INDIVIDUAL/ISOLATE:XYZ2
  - (G) CELL TYPE: unicellular organism
- (vii) IMMEDIATE SOURCE:
  - (A) LIBRARY: genomic
  - (B) CLONE: Para-XYZ2/36
- (x) PUBLICATION INFORMATION:
  - (A) AUTHORS: Doe, Joan X
    Doe, John Q
  - (B) TITLE: Isolation and Characterization of a Gene Encoding a Protease from Paramecium sp.
  - (C) JOURNAL: Fictional Genes
  - (D) VOLUME: I
  - (E) ISSUE: 1
  - (F) PAGES: 1-20
  - (G) DATE: 02-MAR-1988
  - (K) RELEVANT RESIDUES IN SEQ ID NO:1: FROM 1 TO 954

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

```
ATCGGGATAG TACTGGTCAA GACCGGTGGA CACCGGTTAA CCCCGGTTAA GTACCGGTTA    60

TAGGCCATTT CAGGCCAAAT GTGCCCAACT ACGCCAATTG TTTTGCCAAC GGCCAACGTT   120

ACGTTCGTAC GCACGTATGT ACCTAGGTAC TTACGGACGT GACTACGGAC ACTTCCGTAC   180

GTACGTACGT TTACGTACCC ATCCCAACGT AACCACAGTG TGGTCGCAGT GTCCCAGTGT   240

ACACAGACTG CCAGACATTC TTCACAGACA CCCC ATG ACA CCA CCT GAA CGC CTC    295
                                      Met Thr Pro Pro Glu Arg Leu
                                                          -30

TTC CTC CCA AGG GTG TGT GGC ACC ACC CTA CAC CTC CTC CTT CTG GGG      343
Phe Leu Pro Arg Val Cys Gly Thr Thr Leu His Leu Leu Leu Leu Gly
       -25                 -20                 -15

CTG CTG CTG GTT CTG CTG CCT GGG GCC CAT GTGAGGCAGC AGGAGAATGG        393
Leu Leu Leu Val Leu Leu Pro Gly Ala His
  -10                 -5

GGTGGCTCAG CCAAACCTTG AGCCCTAGAG CCCCCCTCAA CTCTGTTCTC CTAG GGG      450
                                                           Gly

CTC ATG CAT CTT GCC CAC AGC AAC CTC AAA CCT GCT GCT CAC CTC ATT      498
Leu Met His Leu Ala His Ser Asn Leu Lys Pro Ala Ala His Leu Ile
1               5                  10                  15

GTAAACATCC ACCTGACCTC CCAGACATGT CCCCACCAGC TCTCCTCCTA CCCCTGCCTC   558

AGGAACCCAA GCATCCACCC CTCTCCCCCA ACTTCCCCCA CGCTAAAAAA AACAGAGGGA   618

GCCCACTCCT ATGCCTCCCC CTGCCATCCC CCAGGAACTC AGTTGTTCAG TGCCCACTTC   678

TAC CCC AGC AAG CAG AAC TCA CTG CTC TGG AGA GCA AAC ACG GAC CGT      726
Tyr Pro Ser Lys Gln Asn Ser Leu Leu Trp Arg Ala Asn Thr Asp Arg
            20                  25                  30

GCC TTC CTC CAG GAT GGT TTC TCC TTG AGC AAC AAT TCT CTC CTG GTC      774
Ala Phe Leu Gln Asp Gly Phe Ser Leu Ser Asn Asn Ser Leu Leu Val
       35                  40                  45

TAGAAAAAAT AATTGATTTC AAGACCTTCT CCCCATTCTG CCTCCATTCT GACCATTTCA   834

GGGGTCGTCA CCACCTCTCC TTTGGCCATT CCAACAGCTC AAGTCTTCCC TGATCAAGTC   894

ACCGGAGCTT TCAAAGAAGG AATTCTAGGC ATCCCAGGGG ACCCACACCT CCCTGAACCA   954
```

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 82 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:

(A) NAME/KEY: signal sequence

(B) LOCATION: −34 to −1

(C) IDENTIFICATION METHOD: similarity to other signal sequences, hydrophobic

(D) OTHER INFORMATION: expresses protease

(x) PUBLICATION INFORMATION:

(A) AUTHORS: Doe, Joan X
Doe, John Q

(B) TITLE: Isolation and Characterization of a Gene Encoding a Protease from Paramecium sp.

(C) JOURNAL: Fictional Genes

(D) VOLUME: I

(E) ISSUE: 1

(F) PAGES: 1−20

(G) DATE: 02−MAR−1988

(K) RELEVANT RESIDUES IN SEQ ID NO:2: FROM −34 TO 48

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Met	Thr	Pro	Pro	Glu	Arg	Leu	Phe	Leu	Pro	Arg	Val	Cys	Gly	Thr	Thr
				−30				−25				−20			
Leu	His	Leu	Leu	Leu	Leu	Gly	Leu	Leu	Leu	Val	Leu	Leu	Pro	Gly	Ala
			−15					−10			−5				
His	Gly	Leu	Met	His	Leu	Ala	His	Ser	Asn	Leu	Lys	Pro	Ala	Ala	His
		1			5				10						
Leu	Ile	Tyr	Pro	Ser	Lys	Gln	Asn	Ser	Leu	Leu	Trp	Arg	Ala	Asn	Thr
15					20				25				30		
Asp	Arg	Ala	Phe	Leu	Gln	Asp	Gly	Phe	Ser	Leu	Ser	Asn	Asn	Ser	Leu
				35				40				45			

Leu Val

2432 Sequence Listing Headings

A complete listing of abbreviated headings for all items of information is provided below. After the heading for each item in the "Sequence Listing," the appropriate information or a yes/no answer should be provided. Where "SEQ ID NO:X" appears, the appropriate sequence identification number should be provided for X.

(1) GENERAL INFORMATION:
- (i) APPLICANT:
- (ii) TITLE OF INVENTION:
- (iii) NUMBER OF SEQUENCES:
- (iv) CORRESPONDENCE ADDRESS:
  - (A) ADDRESSEE:
  - (B) STREET:
  - (C) CITY:
  - (D) STATE:
  - (E) COUNTRY:
  - (F) ZIP:
- (v) COMPUTER READABLE FORM:
  - (A) MEDIUM TYPE:
  - (B) COMPUTER:
  - (C) OPERATING SYSTEM:
  - (D) SOFTWARE:
- (vi) CURRENT APPLICATION DATA :
  - (A) APPLICATION NUMBER:
  - (B) FILING DATE:
  - (C) CLASSIFICATION:
- (vii) PRIOR APPLICATION DATA:
  - (A) APPLICATION NUMBER:
  - (B) FILING DATE:
- (viii) ATTORNEY/AGENT INFORMATION:
  - (A) NAME:
  - (B) REGISTRATION NUMBER:
  - (C) REFERENCE/DOCKET NUMBER:
- (ix) TELECOMMUNICATION INFORMATION:
  - (A) TELEPHONE:
  - (B) TELEFAX:
  - (C) TELEX:

2) INFORMATION FOR SEQ ID NO: X:
- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH:
  - (B) TYPE:
  - (C) STRANDEDNESS:
  - (D) TOPOLOGY:
- (ii) MOLECULE TYPE:
- (iii) HYPOTHETICAL:
- (iv) ANTI-SENSE:
- (v) FRAGMENT TYPE:
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM:
  - (B) STRAIN:
  - (C) INDIVIDUAL ISOLATE:
  - (D) DEVELOPMENTAL STAGE:
  - (E) HAPLOTYPE:
  - (F) TISSUE TYPE:
  - (G) CELL TYPE:
  - (H) CELL LINE:
  - (I) ORGANELLE:
- (vii) IMMEDIATE SOURCE:
  - (A) LIBRARY:
  - (B) CLONE:
- (viii) POSITION IN GENOME:
  - (A) CHROMOSOME/SEGMENT:
  - (B) MAP POSITION:
  - (C) UNITS:
- (ix) FEATURE:
  - (A) NAME/KEY:
  - (B) LOCATION:
  - (C) IDENTIFICATION METHOD:
  - (D) OTHER INFORMATION:
- (x) PUBLICATION INFORMATION:
  - (A) AUTHORS:
  - (B) TITLE:
  - (C) JOURNAL:
  - (D) VOLUME:
  - (E) ISSUE:
  - (F) PAGES:
  - (G) DATE:
  - (H) DOCUMENT NUMBER:
  - (I) FILING DATE:
  - (J) PUBLICATION DATE:
  - (K) RELEVANT RESIDUES :
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:X:

2433 Sequence Listing Headings for Mandatory Items

The Sequence Listing headings for all mandatory items are listed below. It can be seen from this somewhat limited list of information items that full copliance with the rules can be readily achieved by focusing on the mandatory information items.

(1) GENERAL INFORMATION:
(i) APPLICANT:
(ii) TITLE OF INVENTION:
(iii) NUMBER OF SEQUENCES:
(i) APPLICANT: Doe, Joan X
(iv) CORRESPONDENCE ADDRESS:
(A) ADDRESSEE:
(B) STREET:
(C) CITY:
(D) STATE:
(E) COUNTRY:
(F) ZIP:
(v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE:
(B) COMPUTER:
(C) OPERATING SYSTEM:
(D) SOFTWARE:
(vi) CURRENT APPLICATION DATA (If otherwise, heading should still be supplied):
(A) APPLICATION NUMBER:
(B) FILING DATE:
(C) CLASSIFICATION:
(vii) PRIOR APPLICATION DATA (If applicable):
(A) APPLICATION NUMBER:
(B) FILING DATE:
2) INFORMATION FOR SEQ ID NO: X:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:
(B) TYPE:
(C) STRANDEDNESS:
(D) TOPOLOGY:
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:X: