

Chapter 2400 Biotechnology

| | | | |
|-------------|---|--|--|
| 2401 | Introduction | | |
| 2402 | The Deposit Rules | | |
| 2403 | Deposit of Biological Material | | |
| 2403.01 | Material Capable of Self-Replication | | |
| 2403.02 | Plant Material | | |
| 2404 | Need or Opportunity to Make a Deposit | | |
| 2404.01 | Biological Material That Is Known and Readily Available to the Public | | |
| 2404.02 | Biological Material That Can Be Made or Isolated Without Undue Experimentation | | |
| 2404.03 | Reference to a Deposit in the Specification | | |
| 2405 | Acceptable Depository | | |
| 2406 | Time of Making an Original Deposit | | |
| 2406.01 | Description in Application Specification | | |
| 2406.02 | Deposit After Filing Date - Corroboration | | |
| 2406.03 | Possible Loss of U.S. Filing Date in Other Countries | | |
| 2407 | Replacement or Supplement of Deposit | | |
| 2407.01 | In a Pending Application | | |
| 2407.02 | After a Patent Has Issued | | |
| 2407.03 | Failure to Replace | | |
| 2407.04 | Treatment of Replacement | | |
| 2407.05 | Exemption From Replacement | | |
| 2407.06 | Replacement May Not Be Recognized | | |
| 2408 | Term of Deposit | | |
| 2409 | Viability of Deposit | | |
| 2410 | Furnishing of Samples | | |
| 2410.01 | Conditions of Deposit | | |
| 2410.02 | Certification of Statement of Availability of Deposit | | |
| 2411 | Examination Procedures | | |
| 2411.01 | Rejections Based on Deposit Issue | | |
| 2411.02 | Replies to Rejections Based on Deposit Issue | | |
| 2411.03 | Application in Condition for Allowance Except for Deposit | | |
| 2411.04 | After a Patent Has Been Granted | | |
| 2411.05 | Content of Application with Respect to Deposited Material | | |
| 2420 | The Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures - the Sequence Rules | | |
| 2421 | Overview of the Sequence Rules | | |
| 2421.01 | Applications Affected | | |
| 2421.02 | Summary of the Requirements of the Sequence Rules | | |
| 2421.03 | Notification of a Failure to Comply | | |
| 2421.04 | Future Changes to the Sequence Rules | | |
| 2422 | Nucleotide and/or Amino Acid Sequence Disclosures in Patent Applications | | |
| 2422.01 | Definitions of Nucleotide and/or Amino Acids for Purpose of Sequence Rules | | |
| 2422.02 | The Requirement for Exclusive Conformance; Sequences Presented in Drawing Figures | | |
| 2422.03 | The Requirements for a Sequence Listing and Sequence Identifiers; Sequences Embedded in Application Text; Variants of a Presented Sequence | | |
| 2422.04 | The Requirement for a Computer Readable Copy of the Official Copy of the Sequence Listing | | |
| 2422.05 | Reference to Previously Filed Identical Computer Readable Form; Continuing or Derivative Applications; Request for Transfer of Computer Readable Form | | |
| 2422.06 | Requirement for Statement Regarding Content of Official and Computer Readable Copies of Sequence Listing | | |
| 2422.07 | Requirements for Compliance, Statements Regarding New Matter, and Sanctions for Failure to Comply | | |
| 2422.08 | Presumptions Regarding Compliance | | |
| 2422.09 | Box Sequence; Hand Delivery of Sequence Listings and Computer Readable Forms | | |
| 2423 | Symbols and Format To Be Used for Nucleotide and/or Amino Acid Sequence Data | | |
| 2423.01 | Format and Symbols To Be Used in Sequence Listings | | |
| 2423.02 | Depiction of Coding Regions | | |
| 2423.03 | Presentation and Enumeration of Sequences | | |
| 2424 | Requirements for Nucleotide and/or Amino Acid Sequences as Part of the Application Papers | | |
| 2424.01 | Informational Requirements for the Sequence Listing | | |
| 2424.02 | Sequence Listing Numeric Identifiers | | |
| 2424.03 | Additional Miscellaneous Requirements | | |
| 2425 | Form and Format for Nucleotide and/or Amino Acid Sequence Submissions in Computer Readable Form | | |
| 2426 | Amendments to or Replacement of Sequence Listing and Computer Readable Copy Thereof | | |
| 2427 | Form Paragraphs and Notice to Comply | | |
| 2427.01 | Form Paragraphs | | |
| 2427.02 | Notice To Comply | | |
| 2428 | Sample Statements | | |
| 2429 | Helpful Hints for Compliance | | |
| 2430 | Patent Information; Utilities Programs; | | |

Training

- 2431 **Sample Sequence Listing**
- 2434 **Examination of Patent Applications Claiming Large Numbers of Nucleotide Sequences**
- 2435 **Publishing of Patents and Patent Application Publications With Lengthy Sequence Listings**

2401 Introduction

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 FR 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. Revised deposit rules were published in the *Federal Register* at 66 FR 21090 (April 27, 2001) and in the *Official Gazette* at 1246 O.G. 104 (May 22, 2001) and went into effect on May 29, 2001. 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 FR 18230 (May 1, 1990) and in the *Official Gazette*, 1114 O.G. 29 (May 15, 1990) and went into effect on October 1, 1990. Revised sequence rules were published in the *Federal Register* at 63 FR 29620 (June 1, 1998) and in the *Official Gazette* at 1121 O.G. 82 (June 23, 1998) and went into effect on July 1, 1998.

Further revisions to the sequence rules were published in the *Federal Register* at 65 FR 54604 (September 8, 2000) and in the *Official Gazette* at 1238 O.G. 145 (September 19, 2000) and went into effect on September 8, 2000.

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 FR 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 FR 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 FR 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. See also MPEP § 2434.

2402 The Deposit Rules

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. See, e.g., *Ajinomoto Co. v. Archer-Daniels-Midland Co.*, 228 F.3d 1338, 1345-46, 56 USPQ2d 1332, 1337-38 (Fed. Cir. 2000), *cert. denied*, 121 S.Ct. 1957 (2001)(explaining how deposit may help satisfy enablement requirement); *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 Microorganisms 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. See 37 CFR 1.806 (the term of deposit is “at least thirty (30) years and at least five (5) years after the most recent request” for a sample; the agreement sufficiently ensures that the deposit will be “available beyond the enforceable life of the patent”). 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 alone may or may not be sufficient 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. See the final rule entitled “Deposit of Biological Materials for Patent Purposes,” 54 FR 34864, 34875 (August 22, 1989). 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 (37 CFR 1.808(b)), 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. For this reason, 37 CFR 1.808(c) provides that 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. See 37 CFR 1.808(c) and MPEP § 2410.02 for the requirements of the request. The Office will not certify that the aforementioned statement has been made unless

(A) the deposit was necessary to overcome a rejection under 35 U.S.C. 112,

(B) there is, in the record, a statement by the examiner that a rejection would have been made "but for" the deposit (assumes deposit information in record, as filed), or

(C) the record otherwise clearly indicates that the deposit was made under Budapest Treaty, and that 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 (with the possible exception of requiring the request

for the deposit to be in the format specified in 37 CFR 1.808(b)).

If a deposit is not made under the conditions set forth in 37 CFR 1.808(a), 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 USPQ2d 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

37 CFR 1.803. Acceptable depository.

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

(1) any International Depository Authority (IDA) as established under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms 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 para-

graph (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 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, 1998) 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 Microorganisms 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 depository authorities.

CURRENT IDAs

The following constitutes the list of IDAs recognized under the Budapest Treaty. The list is current as of July, 2001.

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

American Type Culture Collection (ATCC)
10801 University Blvd.
Manassas, Virginia 20110-2209
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 Brussels
Belgium

Bureau of Microbiology at Health Canada (BMHC)
Federal Laboratories for Health Canada
Room H5190
1015 Arlington Street
Winnipeg, Manitoba
Canada R3E 3R2

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

Colección Española de Cultivos Tipo (CECT)
Universidad de Valencia
Edificio de Investigación
Campus de Burjasot
46100 Burjasot (Valencia)
Spain

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

Collection of Industrial Yeasts DBVPG
Applied Microbiology Section
Department of Plant Biology
Faculty of Agriculture
University of Perugia
Borgo 20 Giugno, 74
06122 Perugia
Italy

Culture Collection of Algae and Protozoa (CCAP)
Institute of Freshwater Ecology
Windermere Laboratory
Ambleside, Cumbria LA22 0LP
United Kingdom and Dunstaffnage Marine Labora-
tory
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)
Masaryk University
ul. Tvrdeho 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 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

Institute of Agriculture and Food Biotechnology
(IAFB)
Collection of Industrial Microorganisms
Ul. Rakowiecka 36
02-532 Warsaw, Poland

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

International Patent Organism Depository (IPOD)
AIST Tsukuba Central 6
1-1, Higashi 1-chome
Tsukuba-shi, Ibaraki-Ken 305-8566
Japan

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

Korean Collection for Type Cultures (KCTC)
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

Microbial Strain Collection of Latvia (MSCL)
University of Latvia
Faculty of Biology
Blvd. Kronvalda 4
LV-1586 Riga
Latvia

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 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, Food and
Marine Bacteria (NCIMB)
23 St. Machar Drive

Aberdeen AB2 1RY
Scotland, United Kingdom

National Research Center of Antibiotics
Nagatinskaya Street 3-a
Moscow 113105
Russian Federation

Polish Collection of Microorganisms (PCM)
Institute of Immunology and Experimental Therapy
Polish Academy of Sciences
Ul. Weigla 12
53-114 Wroclaw
Poland

Russian Collection of Microorganisms (VKM)
Prospekt Naouki, 5
142292 Puschino (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 must promptly submit a statement from a person in a position to corroborate the fact, stating that the biological material which is deposited is a biological material specifically identified in the application as filed.

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 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.

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 the request:

- (1) Includes a statement of the reason for making the replacement or supplemental deposit;
- (2) Includes a statement from a person in a position to corroborate the fact, and stating that the replacement or supplemental deposit is of a biological material which is identical to that originally deposited;
- (3) Includes a 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 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.

(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.

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) describes 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. See also Article 5 of the Budapest Treaty.

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

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 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 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 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 years after issuance or 26 years after application filing) 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

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 Microorganisms 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 conditions:

(A) 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

(B) 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:

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

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

(C) 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 Statement of Availability 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 U.S. 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 a Director of Technology Center (TC) 1600, and contains the following information:

- (A) the name and address of the depository;
- (B) the accession number given to the deposit;
- (C) the patent number and issue date of the patent referring to the deposit; and
- (D) the name and address of the requesting party.

See also MPEP § 2404.01.

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 legal entitlement to receive samples of deposited microorganisms pursuant to Rule 11.3(a) of

the Regulations under the Budapest Treaty. Copies of this form are available from a TC 1600 Director.

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 reply to a rejection under paragraph (a) of this section by—

(1) In the case of an applicant for patent, either making an acceptable original, replacement, or supplemental deposit, or assuring the Office in writing that an acceptable deposit will be made; 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 nonresponsive. 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, applicant will be notified and given a period of time within which the deposit must be made in order to avoid abandonment. This time period is not extendable under § 1.136(a) or (b) if set forth in a "Notice of Allowability" or in an Office action having a mail date on or after the mail date of a "Notice of Allowability" (see § 1.136(c)).

(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.

(e) Any amendment required by paragraphs (d)(1), (d)(2) or (d)(4) of this section must be filed before or with the payment of the issue fee (see § 1.312).

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 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:

(A) 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.

(B) 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.

(C) 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 (1) 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 (2) 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 at least 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.

(D) 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.

(E) 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 Replies 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 reply, 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 nonresponsive 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, applicant will be notified and given a period of time within which the deposit must be made in order to avoid abandonment. This time period is not extendable under 37 CFR 1.136(a) or (b) if set forth in a "Notice of Allowability" or in an Office action having a mail date on or after the mail date of a "Notice of Allowability" (see 37 CFR 1.136(c)). Failure to make the needed deposit in accordance with this requirement will 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 and address 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. Such an amendment must be filed before or with the payment of the issue fee. Therefore, applicants need to make any necessary deposit of biological material well prior to payment of the issue fee such that the accession number is received with sufficient time remaining to amend the specification as required by 37 CFR 1.809(d) on or before the date the issue fee payment is paid. See 37 CFR 1.809(e).

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. The sequence rules were subsequently revised effective July 1, 1998. See 63 FR 29634 (June 1, 1998) and 1121 O.G. 82 (June 23, 1998).

The sequence rules were further revised on September 8, 2000 to allow submissions of the nucleotide and/or amino acid sequences and associated information on compact discs. See 65 FR 54604 (Sept. 8, 2000) and 1238 O.G. 145 (Sept. 19, 2000). See also MPEP § 608.05 and § 2422.03.

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 filed on or after October 1, 1990. The revised sequence rules apply to most new applications filed on or after July 1, 1998. See the final rule publications as cited in MPEP § 2420 for more detailed applicability information.

The Office encourages voluntary compliance for applications not subject to the 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 defines a “sequence” and a “Sequence Listing” for the purpose of the rules, the requirements for specific symbols, and formats for the “Sequence Listing,” the requirement for a computer readable form (CRF) of the “Sequence Listing,” 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, provided that there are at least 4 “specifically defined” nucleotides or 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. 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. Applications filed on or after November 29, 2000, will be retained in the Office of Initial Patent Examination (OIPE) until any noncompliant sequence listing that renders an application unsuitable for examination is corrected. Deficien-

cies of a more sophisticated nature will likely only be detected by the examiner to whom the application is assigned. Applicant will be notified of any errors or inconsistencies detected by the examiner early in the examination process. 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 30-day period for reply. The period for reply will usually be 2 months when sent during the preexamination processing of an application. However, if the notice is sent out with an Office communication having a longer period for reply, the period for reply may be longer than 2 months, e.g., where the notice is sent with an Office action on the merits setting a 3-month period for reply. 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 reply 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 applicant may be given a new time period to correct the omission. 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 through § 2427.02.

A notification of a failure to comply with the sequence rules will be accompanied by an analysis of any 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 Chemical/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 certain forms of electronic media, 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 are 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. Sequences with fewer than four specifically defined nucleotides or amino acids are specifically excluded from this section. "Specifically defined" means those amino acids other than "Xaa" and those nucleotide bases other than "n" defined in accordance with the World Intellectual Property Organization (WIPO) Handbook on Industrial Property Information and Documentation, Standard ST.25: Standard for the Presentation of Nucleotide and Amino Acid Sequence Listings in Patent Applications (1998), including Tables 1 through 6 in Appendix 2, herein incorporated by reference. (Hereinafter "WIPO Standard ST.25 (1998)"). This incorporation by reference was approved by the Director of the Federal Register in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies of WIPO Standard ST.25 (1998) may be obtained from the World Intellectual Property Organization; 34 chemin des Colombettes; 1211 Geneva 20 Switzerland. Copies of ST.25 may be inspected at the Patent Search Room; Crystal Plaza 3, Lobby Level; 2021 South Clark Place; Arlington, VA 22202. Copies may also be inspected at the Office of the Federal Register, 800 North Capitol Street,

NW, Suite 700, Washington, DC. Nucleotides and amino acids are further defined as follows:

(1) *Nucleotides*: Nucleotides are intended to embrace only those nucleotides that can be represented using the symbols set forth in WIPO Standard ST.25 (1998), Appendix 2, Table 1. Modifications, e.g., methylated bases, may be described as set forth in WIPO Standard ST.25 (1998), Appendix 2, Table 2, but shall not be shown explicitly in the nucleotide sequence.

(2) *Amino acids*: Amino acids are those L-amino acids commonly found in naturally occurring proteins and are listed in WIPO Standard ST.25 (1998), Appendix 2, Table 3. 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 WIPO Standard ST.25 (1998), Appendix 2, Table 3 with the modified positions; e.g., hydroxylations or glycosylations, being described as set forth in WIPO Standard ST.25 (1998), Appendix 2, Table 4, 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 WIPO Standard ST.25 (1998), Appendix 2, Table 3 in conjunction with a description in the Feature section 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, a paper copy disclosing 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. This paper copy is hereinafter referred to as the "Sequence Listing." Each sequence disclosed must appear separately in the "Sequence Listing." Each sequence set forth in the "Sequence Listing" shall be assigned a separate sequence identifier. The sequence identifiers shall begin with 1 and increase sequentially by integers. If no sequence is present for a sequence identifier, the code "000" shall be used in place of the sequence. The response for the numeric identifier <160> shall include the total number of SEQ ID NOs, whether followed by a sequence or by the code "000."

(d) Where the description or claims of a patent application discuss a sequence 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 sequence identifier, preceded by "SEQ ID NO:" 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 a 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 Patent and Trademark 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 if the computer readable form in the other application was compliant with all of the requirements of these rules. 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. In the new application, applicant must also request the use of the compliant computer readable "Sequence Listing" that is already on file for the other application and must state that the paper copy of the "Sequence Listing" in the new application is identical to the computer readable copy filed for the other application.

(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, *e.g.*, a statement that "the information recorded in computer readable form is identical to the written sequence listing."

(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(a) or at the time of entering the national stage under 35 U.S.C. 371, applicant will be notified and given a period of time within which to comply with such requirements in order to prevent abandonment of the application. Any submission in reply to a requirement under this paragraph must be accompanied by a statement that the submission includes no new matter.

(h) If any of the requirements of paragraphs (b) through (f) of this section are not satisfied at the time of filing an international application under the Patent Cooperation Treaty (PCT), which application is to be searched by the United States International Searching Authority or examined by the United States International Preliminary Examining Authority, applicant will be sent a notice necessitating compliance with the requirements within a prescribed time period. Any submission in reply to a requirement under this paragraph must be accompanied by a statement that the submission does not include matter which goes beyond the disclosure in the international application as filed. If applicant fails to timely provide the required computer readable form, the United States International Searching Authority shall search only to the extent that a meaningful search can be performed without the computer readable form and the United States International Preliminary Examining Authority shall examine only to the extent that a meaningful examination can be performed without the computer readable form.

37 CFR 1.821 incorporates by reference the World Intellectual Property Organization (WIPO) Handbook on Industrial Property Information and Documentation, Standard ST.25 (1998), including Tables 1 through 6 of Appendix 2. Copies may be obtained from the World Intellectual Property Organization; 34

chemin des Colombettes; 1211 Geneva 20 Switzerland. Copies may be inspected at the Patent Search Room; Crystal Plaza 3, Lobby Level; 2021 South Clark Place; Arlington, VA 22202. Copies may also be inspected at the Office of the Federal Register, 800 North Capitol Street, NW, Suite 700, Washington, DC 20408. These tables are reproduced below.

WIPO Standard ST.25 (1998), Appendix 2, Table 1, provides that the bases of a nucleotide sequence should be represented using the following one-letter code for nucleotide sequence characters:

Table 1: List of Nucleotides

| Symbol | Meaning | Origin of designation |
|--------|---------------------------------------|--------------------------------------|
| a | a | <u>a</u> denine |
| g | g | <u>g</u> uanine |
| c | c | <u>c</u> ytosine |
| t | t | <u>t</u> hymine |
| u | u | <u>u</u> racil |
| r | g or a | <u>p</u> urine |
| y | t/u or c | <u>p</u> yrimidine |
| m | a or c | <u>a</u> mino |
| k | g or t/u | <u>k</u> eto |
| s | g or c | <u>s</u> trong interactions 3H-bonds |
| w | a or t/u | <u>w</u> eak interactions 2H-bonds |
| b | g or c or t/u | not a |
| d | a or g or t/u | not c |
| h | a or c or t/u | not g |
| v | a or g or c | not t, not u |
| n | a or g or c or t/u, unknown, or other | <u>a</u> ny |

WIPO Standard ST.25 (1998), Appendix 2, Table 2, provides that modified bases may be represented as

the corresponding unmodified bases in the sequence itself, if the modified base is one of those listed below and the modification is further described in the Feature section of the Sequence Listing. The codes from the list below may be used in the description (i.e., the specification and drawing, or in the Sequence Listing) but these codes may not be used in the sequence itself.

Table 2: List of Modified Nucleotides

| Symbol | Meaning |
|----------|--|
| ac4c | 4-acetylcytidine |
| chm5u | 5-(carboxyhydroxymethyl)uridine |
| cm | 2'-O-methylcytidine |
| cmnm5s2u | 5-carboxymethylaminomethyl-2-thiouridine |
| cmnm5u | 5-carboxymethylaminomethyluridine |
| d | dihydrouridine |
| fm | 2'-O-methylpseudouridine |
| gal q | beta, D-galactosylqueuosine |
| 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-mannosylqueuosine |
| 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-methylcarbamoyl)threonine |
| mv | uridine-5-oxyacetic acid-methylester |
| o5u | uridine-5-oxyacetic acid |
| osyw | wybutoxosine |
| p | pseudouridine |
| q | queuosine |
| s2t | 5-methyl-2-thiouridine |
| 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-carboxy-propyl)uridine, (acp3)u |

WIPO Standard ST.25 (1998), Appendix 2, Table 3, provides that the amino acids should be represented using the following three-letter code with the first letter as a capital.

Table 3: List of Amino Acids

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

WIPO Standard ST.25 (1998), Appendix 2, Table 4, provides that modified and unusual amino acids may

be represented as the corresponding unmodified amino acids in the sequence itself if the modified or unusual amino acid is one of those listed below and the modification is further described in the Feature section of the Sequence Listing. The codes from the list below may be used in the description (i.e., the specification and drawings, or in Sequence Listing) but these codes may not be used in the sequence itself.

Table 4: List of Modified and Unusual Amino Acids

| Symbol | Meaning |
|--------|--|
| Aad | 2-Aminoadipic acid |
| bAad | 3-Aminoadipic acid |
| bAla | beta-Alanine, beta-Aminopropionic 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 |
| alle | allo-Isoleucine |
| MeGly | N-Methylglycine, sarcosine |
| MeIle | N-Methylisoleucine |
| MeLys | 6-N-Methyllysine |
| MeVal | N-Methylvaline |

| | |
|-----|------------|
| Nva | Norvaline |
| Nle | Norleucine |
| Orn | Ornithine |

WIPO Standard ST.25 (1998), Appendix 2, Table 5, provides for feature keys related to DNA sequences.

Table 5: List of Feature Keys Related to Nucleotide Sequences

| Key | Description |
|-------------|---|
| allele | a related individual or strain contains stable, alternative forms of the same gene which differs from the presented sequence at this location (and perhaps others) |
| attenuator | (1) region of DNA at which regulation of termination of transcription occurs, which controls the expression of some bacterial operons; (2) sequence segment located between the promoter and the first structural gene that causes partial termination of transcription |
| C_region | constant region of immunoglobulin light and heavy chains, and T-cell receptor alpha, beta, and gamma chains; includes one or more exons depending on the particular chain |
| CAAT_signal | CAAT box; part of a conserved sequence located about 75 bp up-stream of the start point of eukaryotic transcription units which may be involved in RNA polymerase binding; consensus=GG (C or T) CAATCT |
| CDS | coding sequence; sequence of nucleotides that corresponds with the sequence of amino acids in a protein (location includes stop codon); feature includes amino acid conceptual translation |
| conflict | independent determinations of the "same" sequence differ at this site or region |
| D-loop | displacement loop; a region within mitochondrial DNA in which a short stretch of RNA is paired with one strand of DNA, displacing the original partner DNA strand in this region; also used to describe the displacement of a region of one strand of duplex DNA by a single stranded invader in the reaction catalyzed by RecA protein |
| D-segment | diversity segment of immunoglobulin heavy chain, and T-cell receptor beta chain |
| enhancer | a cis-acting sequence that increases the utilization of (some) eukaryotic promoters, and can function in either orientation and in any location (upstream or downstream) relative to the promoter |

| Key | Description |
|-----------------|---|
| exon | region of genome that codes for portion of spliced mRNA; may contain 5'UTR, all CDSs, and 3'UTR |
| GC_signal | GC box; a conserved GC-rich region located upstream of the start point of eukaryotic transcription units which may occur in multiple copies or in either orientation; consensus=GGGCGG |
| gene | region of biological interest identified as a gene and for which a name has been assigned |
| iDNA | intervening DNA; DNA which is eliminated through any of several kinds of recombination |
| intron | a segment of DNA that is transcribed, but removed from within the transcript by splicing together the sequences (exons) on either side of it |
| J_segment | joining segment of immunoglobulin light and heavy chains, and T-cell receptor alpha, beta, and gamma chains |
| LTR | long terminal repeat, a sequence directly repeated at both ends of a defined sequence, of the sort typically found in retroviruses |
| mat_peptide | mature peptide or protein coding sequence; coding sequence for the mature or final peptide or protein product following post-translational modification; the location does not include the stop codon (unlike the corresponding CDS) |
| misc_binding | site in nucleic acid which covalently or non-covalently binds another moiety that cannot be described by any other Binding key (primer_bind or protein_bind) |
| misc_difference | feature sequence is different from that presented in the entry and cannot be described by any other Difference key (conflict, unsure, old_sequence, mutation, variation, allele, or modified_base) |
| misc_feature | region of biological interest which cannot be described by any other feature key; a new or rare feature |
| misc_recomb | site of any generalized, site-specific or replicative recombination event where there is a breakage and reunion of duplex DNA that cannot be described by other recombination keys (iDNA and virion) or qualifiers of source key (/insertion_seq, /transposon, /proviral) |
| misc_RNA | any transcript or RNA product that cannot be defined by other RNA keys (prim_transcript, precursor_RNA, mRNA, 5'clip, 3'clip, 5'UTR, 3'UTR, exon, CDS, sig_peptide, transit_peptide, mat_peptide, intron, polyA_site, rRNA, tRNA, scRNA, and snRNA) |
| misc_signal | any region containing a signal controlling or altering gene function or expression that cannot be described by other Signal keys (promoter, CAAT_signal, TATA_signal, -35_signal, -10_signal, GC_signal, RBS, polyA_signal, enhancer, attenuator, terminator, and rep_origin) |

| Key | Description |
|-----------------|--|
| misc_structure | any secondary or tertiary structure or conformation that cannot be described by other Structure keys (stem_loop and D-loop) |
| modified_base | the indicated nucleotide is a modified nucleotide and should be substituted for by the indicated molecule (given in the mod_base qualifier value) |
| mRNA | messenger RNA; includes 5' untranslated region (5'UTR), coding sequences (CDS, exon) and 3' untranslated region (3'UTR) |
| mutation | a related strain has an abrupt, inheritable change in the sequence at this location |
| N_region | extra nucleotides inserted between rearranged immunoglobulin segments |
| old_sequence | the presented sequence revises a previous version of the sequence at this location |
| polyA_signal | recognition region necessary for endonuclease cleavage of an RNA transcript that is followed by polyadenylation; consensus=AATAAA |
| polyA_site | site on an RNA transcript to which will be added adenine residues by post-transcriptional polyadenylation |
| precursor_RNA | any RNA species that is not yet the mature RNA product; may include 5' clipped region (5'clip), 5' untranslated region (5'UTR), coding sequences (CDS, exon), intervening sequences (intron), 3' untranslated region (3'UTR), and 3' clipped region (3'clip) |
| prim_transcript | primary (initial, unprocessed) transcript; includes 5' clipped region (5'clip), 5' untranslated region (5'UTR), coding sequences (CDS, exon), intervening sequences (intron), 3' untranslated region (3'UTR), and 3' clipped region (3'clip) |
| primer_bind | non-covalent primer binding site for initiation of replication, transcription, or reverse transcription; includes site(s) for synthetic, for example, PCR primer elements |
| promoter | region on a DNA molecule involved in RNA polymerase binding to initiate transcription |
| protein_bind | non-covalent protein binding site on nucleic acid |
| RBS | ribosome binding site |
| repeat_region | region of genome containing repeating units |
| repeat_unit | single repeat element |
| rep_origin | origin of replication; starting site for duplication of nucleic acid to give two identical copies |
| rRNA | mature ribosomal RNA; the RNA component of the ribonucleoprotein particle (ribosome) which assembles amino acids into proteins |

| Key | Description |
|-----------------|--|
| S_region | switch region of immunoglobulin heavy chains; involved in the rearrangement of heavy chain DNA leading to the expression of a different immunoglobulin class from the same B-cell |
| satellite | many tandem repeats (identical or related) of a short basic repeating unit; many have a base composition or other property different from the genome average that allows them to be separated from the bulk (main band) genomic DNA |
| scRNA | small cytoplasmic RNA; any one of several small cytoplasmic RNA molecules present in the cytoplasm and (sometimes) nucleus of a eukaryote |
| sig_peptide | signal peptide coding sequence; coding sequence for an N-terminal domain of a secreted protein; this domain is involved in attaching nascent polypeptide to the membrane; leader sequence |
| snRNA | small nuclear RNA; any one of many small RNA species confined to the nucleus; several of the snRNAs are involved in splicing or other RNA processing reactions |
| source | identifies the biological source of the specified span of the sequence; this key is mandatory; every entry will have, as a minimum, a single source key spanning the entire sequence; more than one source key per sequence is permissible |
| stem_loop | hairpin; a double-helical region formed by base-pairing between adjacent (inverted) complementary sequences in a single strand of RNA or DNA |
| STS | Sequence Tagged Site; short, single-copy DNA sequence that characterizes a mapping landmark on the genome and can be detected by PCR; a region of the genome can be mapped by determining the order of a series of STSs |
| TATA_signal | TATA box; Goldberg-Hogness box; a conserved AT-rich septamer found about 25 bp before the start point of each eukaryotic RNA polymerase II transcript unit which may be involved in positioning the enzyme for correct initiation; consensus=TATA(A or T)A(A or T) |
| terminator | sequence of DNA located either at the end of the transcript or adjacent to a promoter region that causes RNA polymerase to terminate transcription; may also be site of binding of repressor protein |
| transit_peptide | transit peptide coding sequence; coding sequence for an N-terminal domain of a nuclear-encoded organellar protein; this domain is involved in post-translational import of the protein into the organelle |
| tRNA | mature transfer RNA, a small RNA molecule (75-85 bases long) that mediates the translation of a nucleic acid sequence into an amino acid sequence |
| unsure | author is unsure of exact sequence in this region |
| V_region | variable region of immunoglobulin light and heavy chains, and T-cell receptor alpha, beta, and gamma chains; codes for the variable amino terminal portion; can be made up from V_segments, D_segments, N_regions, and J_segments |

| Key | Description |
|------------|---|
| V_segment | variable segment of immunoglobulin light and heavy chains, and T-cell receptor alpha, beta, and gamma chains; codes for most of the variable region (V_region) and the last few amino acids of the leader peptide |
| variation | a related strain contains stable mutations from the same gene (for example, RFLPs, polymorphisms, etc.) which differ from the presented sequence at this location (and possibly others) |
| 3'clip | 3'-most region of a precursor transcript that is clipped off during processing |
| 3'UTR | region at the 3' end of a mature transcript (following the stop codon) that is not translated into a protein |
| 5'clip | 5'-most region of a precursor transcript that is clipped off during processing |
| 5'UTR | region at the 5' end of a mature transcript (preceding the initiation codon) that is not translated into a protein |
| -10_signal | pribnow box; a conserved region about 10 bp upstream of the start point of bacterial transcription units which may be involved in binding RNA polymerase; consensus=TAtAaT |
| -35_signal | a conserved hexamer about 35 bp upstream of the start point of bacterial transcription units; consensus=TTGACa [] or TGTTGACA [] |

WIPO Standard ST.25 (1998), Appendix 2, Table 6 provides for feature keys related to protein sequences

Table 6: List of Feature Keys Related to Protein Sequences

| Key | Description |
|-------------|---|
| CONFLICT | different papers report differing sequences |
| VARIANT | authors report that sequence variants exist |
| VARSPLIC | description of sequence variants produced by alternative splicing |
| MUTAGEN | site which has been experimentally altered |
| MOD_RES | post-translational modification of a residue |
| ACETYLATION | N-terminal or other |
| AMIDATION | generally at the C-terminal of a mature active peptide |
| BLOCKED | undetermined N- or C-terminal blocking group |
| FORMYLATION | of the N-terminal methionine |

| | |
|--|--|
| GAMMA-CARBOXYGLUTAMIC ACID HYDROXYLATION | of asparagine, aspartic acid, proline or lysine |
| METHYLATION | generally of lysine or arginine |
| PHOSPHORYLATION | of serine, threonine, tyrosine, aspartic acid or histidine |
| PYRROLIDONE CARBOXYLIC ACID | N-terminal glutamate which has formed an internal cyclic lactam |
| SULFATATION | generally of tyrosine |
| LIPID | covalent binding of a lipidic moiety |
| MYRISTATE | myristate group attached through an amide bond to the N-terminal glycine residue of the mature form of a protein or to an internal lysine residue |
| PALMITATE | palmitate group attached through a thioether bond to a cysteine residue or through an ester bond to a serine or threonine residue |
| FARNESYL | farnesyl group attached through a thioether bond to a cysteine residue |
| GERANYL-GERANYL | geranyl-geranyl group attached through a thioether bond to a cysteine residue |
| GPI-ANCHOR | glycosyl-phosphatidylinositol (GPI) group linked to the alpha-carboxyl group of the C-terminal residue of the mature form of a protein |
| N-ACYL DIGLYCERIDE | N-terminal cysteine of the mature form of a prokaryotic lipoprotein with an amide-linked fatty acid and a glyceryl group to which two fatty acids are linked by ester linkages |
| DISULFID | disulfide bond; the 'FROM' and 'TO' endpoints represent the two residues which are linked by an intra-chain disulfide bond; if the 'FROM' and 'TO' endpoints are identical, the disulfide bond is an interchain one and the description field indicates the nature of the cross-link |
| THIOLEST | thiolester bond; the 'FROM' and 'TO' endpoints represent the two residues which are linked by the thiolester bond |
| THIOETH | thioether bond; the 'FROM' and 'TO' endpoints represent the two residues which are linked by the thioether bond |
| CARBOHYD | glycosylation site; the nature of the carbohydrate (if known) is given in the description field |
| METAL | binding site for a metal ion; the description field indicates the nature of the metal |

| | |
|----------|---|
| BINDING | binding site for any chemical group (co-enzyme, prosthetic group, etc.); the chemical nature of the group is given in the description field |
| SIGNAL | extent of a signal sequence (prepeptide) |
| TRANSIT | extent of a transit peptide (mitochondrial, chloroplastic, or for a microbody) |
| PROPEP | extent of a propeptide |
| CHAIN | extent of a polypeptide chain in the mature protein |
| PEPTIDE | extent of a released active peptide |
| DOMAIN | extent of a domain of interest on the sequence; the nature of that domain is given in the description field |
| CA_BIND | extent of a calcium-binding region |
| DNA_BIND | extent of a DNA-binding region |
| NP_BIND | extent of a nucleotide phosphate binding region; the nature of the nucleotide phosphate is indicated in the description field |
| TRANSMEM | extent of a transmembrane region |
| ZN_FING | extent of a zinc finger region |
| SIMILAR | extent of a similarity with another protein sequence; precise information, relative to that sequence is given in the description field |
| REPEAT | extent of an internal sequence repetition |
| HELIX | secondary structure: Helices, for example, Alpha-helix, 3(10) helix, or Pi-helix |
| STRAND | secondary structure: Beta-strand, for example, Hydrogen bonded beta-strand, or Residue in an isolated beta-bridge |
| TURN | secondary structure: Turns, for example, H-bonded turn (3-turn, 4-turn, or 5-turn) |
| ACT_SITE | amino acid(s) involved in the activity of an enzyme |
| SITE | any other interesting site on the sequence |
| INIT_MET | the sequence is known to start with an initiator methionine |

