AIPLA
AMERICAN INTELLECTUAL PROPERTY LAW ASSOCIATION

July 16, 2012

The Honorable David J. Kappos
Under Secretary of Commerce for Intellectual Property and
Director of the United States Patent and Trademark Office
United States Patent and Trademark Office
600 Dulany Street
Alexandria, VA 22314

Via email: seq_listing_xml@uspto.gov

RE: **Request for Comments on the Recommendation for the Disclosure of Sequence Listings Using XML (Proposed WIPO ST.26) 77 Fed. Reg. 28541 (May 15, 2012)**

Dear Under Secretary Kappos:

The American Intellectual Property Law Association (AIPLA) appreciates this opportunity to provide comments about the Recommendation for the Disclosure of Sequence Listings Using XML (Proposed WIPO ST.26 standard), published in the Federal Register on May 15, 2012 (77 Fed. Reg. 28541).

AIPLA is a U.S.-based national bar association with approximately 14,000 members who are primarily lawyers in private and corporate practice, government service, and the academic community. AIPLA represents a diverse spectrum of individuals, companies, and institutions involved directly and indirectly in the practice of patent, trademark, copyright, unfair competition, and trade secret law, as well as other fields of law affecting intellectual property. Our members practice or are otherwise involved in patent law and other intellectual property law in the United States and in jurisdictions throughout the world.

About 1,200 of AIPLA's members belong to our Biotechnology Committee, whose members have a high level of interest in the Recommendation because it would affect their practices and could affect costs for their clients.

AIPLA supports the aspirations underlying the Proposed WIPO ST.26 standard for Sequence Listings. Enhanced accuracy, acceptance by all patent offices, and compatibility with other database providers, if achieved cost-effectively with a relatively smooth transition, would be valuable to AIPLA's members and to our members' clients. AIPLA recognizes and appreciates the incentives and expected benefits of moving to the new standard. Nevertheless, a substantial number of members consider the current WIPO ST.25 (ST.25) standard to be sufficient. In addition, AIPLA is concerned that compliance with the Proposed WIPO ST.26 standard will be burdensome and questions whether some requirements could be met in practice. Still further, AIPLA has concerns about increased costs and complexities for applicants to comply with the Proposed WIPO ST.26 standard.

AIPLA specifically comments about the following items, as numbered in the proposal: (1) Comprehensiveness and Clarity, (3) Feature Keys and Qualifiers, (4) Definition of a Sequence for which a Sequence Listing is Required, and (6) Transition Issues.

(1) Comprehensiveness and Clarity.

As a general matter, the main body of the Proposed WIPO ST.26 standard may not be sufficiently comprehensive and clear to achieve the stated goal of permitting an applicant to draw up a single sequence listing and have it be accepted in all international, regional, and national patent offices. Even if the new standard is adopted and WIPO, EPO, USPTO, and JPO agree that the XML and any additional sequence data do not have to be translated, there is no guarantee that other countries will not require translations. The XML file under the Proposed WIPO ST.26 standard is expected to be about 5–10 times longer than a sequence listing under the present WIPO ST.25 standard, which is very widely, if not uniformly, accepted without translation and extra fees. Foreign translation costs as well as extra page fees for such additional information are significant uncertainties that cause AIPLA concern. Without guarantees that all WIPO member countries will accept the sequence listing produced under the Proposed WIPO ST.26 standard, the new standard may create burden without sufficient off-setting benefit.

With respect to our specific concerns, clarification is requested regarding use of the symbol "X" as a residue within a sequence. Paragraph 20 of the Proposed WIPO ST.26 standard seems ambiguous when taken in the context of other aspects of the standard: "The symbol 'X' is the equivalent of only one modified amino acid." Does this mean that X cannot represent a variable position with various alternate options of single amino acid substitutions, peptide substitutions, or that the position can lack an amino acid? Under the Proposed WIPO ST.26 standard, does "only one modified amino acid" mean that each possible amino acid in the string of amino acids at X must be listed singly in a separate sequence with its own SEQ ID number?

A related concern is whether sequence listings will be required for species only, but not for generic descriptions, such as those that commonly appear in claims. As an example of the uncertainty, suppose that an applicant has identified a number of variants of Peptide X that have improved properties and wants to claim them as a small genus around the disclosed species. Peptide X is an 18-mer having the sequence "AIPLAISTHEIPLEADER." On the basis of knowledge in the art and on having made and tested 15 specific variants of Peptide X, all of which are specifically disclosed in the application, the applicant may want to claim a genus of variants as: $AX_1PLAX_2STHEX_3PLEADER$, where X_1 is I, A, F, Y, or is absent; X_2S is I, V, L, or M; and X_3 is I, D, E, N, or Q, provided that X_1, X_2, and X_3 are not all I. The genus encompasses 79 species. There is no uncertainty that each of the 15 disclosed peptide variants would require a separate SEQ ID NO.

Under the Proposed WIPO ST.26 standard, would a SEQ ID NO or multiple SEQ ID NOs be required for the generic description? If so, would a single SEQ ID NO be assigned for the sequence "$AX_1PLAX_2STHEX_3PLEADER$," with Xs defined as above? Or, would a single SEQ ID NO be assigned for the sequence "$AX_1PLAX_2STHEX_3PLEADER$" and a set of

substitutions be defined in the VARIABLE feature? Or, would 79 SEQ ID NOs have to be individually assigned and described? If 79 SEQ ID NOs will be required, then the Proposed WIPO ST.26 standard is highly inefficient compared with the current ST.25 standard for many realistic scenarios in which the invention involves substitutions at multiple positions.

Clarification of whether a sequence code is required for a generic description is requested. Adding several examples to demonstrate how to apply the Proposed WIPO ST.26 standard in disclosing and claiming structure-activity relationships for peptides and proteins will be essential.

(3) Feature Keys and Qualifiers.

The proposed features and qualifiers available for annotation of a sequence under the Proposed WIPO ST.26 standard are generally useful. However, it may be burdensome to prepare and adequately review a Sequence Listing in XML format, such that the potential benefits of the Proposed WIPO ST.26 standard may not outweigh its burden.

AIPLA would also be concerned if WIPO revised the feature keys and qualifiers more frequently than about every 5 years, because of the burdens placed on the USPTO and on practitioners with respect to rule changes. A significant benefit of the current ST.25 standard has been the infrequency of changes over the 14 years it has been in effect. The concern is not that the software will have to be updated, but that practitioners and staff may have to adapt too frequently to updates and changes not driven by the patent system.

(4) Definition of a Sequence for which a Sequence Listing is Required.

(a) Prohibited Sequences. Paragraph 4 of the Proposed WIPO ST.26 standard states: "A sequence listing shall not include any branched nucleotide or amino acid sequences or any sequences with fewer than ten specifically defined nucleotides or fewer than four specifically defined amino acids." Branched sequences may be listed under the current ST.25 standard by describing the location of the branching as a modified residue, and listing the moiety or chain which modifies that residue. Even multiple branch chains can be described. However, under the Proposed WIPO ST.26 standard, the addition of even one branched moiety on a sequence prohibits the listing of that sequence. We request guidance as to how such sequences are to be accurately set forth in the application following adoption of the Proposed WIPO ST.26 standard.

(d) Variants. Related to the comments above about clarity, AIPLA requests clarification about the meaning and proper use of the "variant" feature under the Proposed WIPO ST.26 standard. Under the current standard, this feature is used inconsistently by practitioners and applicants. Some use this feature to define variable amino acids or nucleotides within a sequence. Others list the same genus using the feature "misc_feature" as opposed to "variant." Both are allowable under the current ST.25 standard, yet it is unclear which description is correct or preferred.

The Proposed WIPO ST.26 standard does not seem to resolve this ambiguity. In fact, the example shown for "VARIANT" may introduce more ambiguity because it only demonstrates a sequence having a single alternate amino acid, at a single position. If the sequence represented a genus, then would multiple sequence ID numbers be required under the Proposed WIPO ST.26 standard, each listing a single variable at each specific position? Alternatively, would it be acceptable to have the genus sequence listed, containing X in each location in which a variable occurs, but also to have multiple VARIANT feature keys, each listing one of the possible amino acids which may occur at a specific position? A third alternative would be to use the VARIANT feature key, but list the multiple choices for amino acid at that position.

AIPLA has significant concerns whether practitioners could meet the additional requirements under the Proposed WIPO ST.26 standard with respect to sequence variants. In particular, the requirement that all sequence variants specifically mentioned in the specification be set forth in the sequence listing as individual sequences having their own SEQ ID NOs would be burdensome. Similarly, the requirement that all sequence variants disclosed in the specification only by reference to a primary sequence in the Sequence Listing (e.g., deletions, additions, or substitutions) be set forth in the Sequence Listing as individual sequences having their own SEQ ID NOs or by annotation of the primary sequence as features/qualifiers would also be burdensome. This latter requirement also limits the ability of staff or technical personnel (i.e., individuals other than a registered practitioner) to prepare Sequence Listings. Under the current standard, individuals unfamiliar with the content of an application can simply scan the application for nucleotide and amino acid disclosures of a minimal length for inclusion in the Sequence Listing. Indeed, this is a function currently performed by the Office of Initial Patent Examination. The additional requirements of the Proposed WIPO ST.26 standard will require that registered practitioners consider non-sequence, textual disclosure to assess whether additional sequences or annotations should be included in a Sequence Listing.

(6) Transition Issues.

The effective date should be set no sooner than one year following publication of the final rule. AIPLA favors a "clean" transition date. However, compliance with the new standard should not be required for obtaining a filing date. Specifically, applicants should be allowed to submit an application containing nucleotide and/or amino acid sequence disclosures in any format, with an Official Communication requesting submission of a Sequence Listing complying with the new standard to be issued thereafter as part of preexamination processing. In addition, continuing applications and other applications containing a sequence listing in the current ST.25 standard, which are relied upon for priority/benefit, should be allowed to proceed under the current ST.25 standard or the new standard at an applicant's discretion. A continuing application filed after the effective date, which claims priority to an application having a Sequence Listing filed according to the current ST.25 standard, should benefit from continued availability of a request under 37 CFR 1.821(e).

AIPLA urges that a software tool that easily and completely converts between the current ST.25 standard and any new standard be made available well before the effective date so that applicants, practitioners, and support staff may have sufficient time to become familiar with its operation and to develop confidence in their ability to understand the format of the new standard. Such a tool should be available at no cost or at nominal cost.

AIPLA also urges that applicants be permitted to additionally include sequence data in any format (e.g., in the text of Examples, in Drawings, or as a Sequence Listing under the current ST.25), which may be fully relied upon for support and/or correction of an initial and/or substitute Sequence Listing under the new standard, if needed. Given the critical nature of sequence data to the claimed invention of many biotechnology applications, and the potential for error when generating a Sequence Listing, most practitioners currently include such "duplicative" sequences. Application pages that only set forth sequence data should not be counted in a calculation to assess application size fees, or otherwise create additional fees.

AIPLA appreciates the opportunity to present comments on these important issues and would be happy to answer any questions they may raise.

Sincerely,

William G. Barber
President
American Intellectual Property Law Association