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-- October 2009

***Via E-mail as Attachment***

Susan K. Fawcett
Records Officer
Office of the Chief Information Officer
Administrative Management Group
United States Patent and Trademark Office
P. O. Box 1450
Alexandria, VA 22313-1450

Re: 0651-0024
Requirements for Patent Applications Containing Nucleotide Sequences and/or Amino Acid Sequence Disclosures

Dear Ms. Fawcett:

I am Chief Legal Officer for Palatin Technologies, Inc., a publicly-traded biotechnology company (NYSE Amex: PTN). As Chief Legal Officer, among other duties I am responsible for our patent portfolio, and I am attorney of record on a number of patent applications before the USPTO.

I have filed a number of cases involving either synthetic peptides (amino acid sequences chemically synthesized from individual amino acids, many of which are cyclic and frequently contain either D-amino acids and/or non-coded amino acids) or peptidomimetics (compounds which contain a synthetic peptide sequence, frequently with either D-amino acids and/or non-coded amino acids, and a non-peptide component, typically a small molecule component). None of these cases involve amino acid sequences made by translation of mRNA, and the vast majority of disclosed synthetic peptides either could not be made, or could not practically be made, by means of translation of mRNA, even by means of posttranslational modification.

<u>General Comment on Collection of Information</u>

It is apparent, both historically and from relevant portions of the MPEP and sequence listing rules, that coded amino acid sequences, made by translation of mRNA, were and are the primary focus. For example, amino acid sequences containing D-amino acids are specifically excluded (37 CFR 1.821(a)(2)), and any non-coded amino acid is listed as “Xaa”, with the identity of the non-coded amino acid disclosed only in the feature sequence of the sequence listing.

Even though the apparent focus of the amino acid sequence disclosure requirement is on coded amino acid sequences, the ambit of the rules are broader, and encompass some, but not all, classes of synthetic amino acid sequences. This frequently leads to anomalous results; for example, I have filed some patent applications which contain several hundred amino acid sequences, but of the several hundred sequences only a subset, for example fifty sequences, are required to be disclosed on a sequence listing. The remaining sequences are excluded, typically because the sequences contain D-amino acids or are branched sequences.

It is difficult to effectively search the prior art for peptides or proteins which contain non-coded amino acids. Most chemical compound databases, such as CAS REGISTRY database, the Chemistry Resource component of the Derwent World Patents Index database, the Beilstein database and the Merged Markush Service database, are useful, if at all, only for small peptides, containing no more than six or seven amino acids. Protein databases, including Swissprot, Protein Data Bank and patented protein sequences, are limited to coded amino acids, and cannot be searched for non-coded amino acid or, in the case of peptidomimetic compounds, for non-amino acid components.

Because sequence listings are limited to coded amino acids, the information in sequence listings containing non-coded amino acids, which non-coded amino acids are required to be listed as "X" or "Xaa", is generally useless. For example, assume a seven amino acid sequence, which is asserted to be novel based on non-coded amino acids in two positions. The amino acid sequence disclosures will not capture any useful information relating to the non-coded amino acids, and if the sequence of five coded amino acids is conventional and well known in the art, there may well be hundreds or thousands of protein database entries which will match.

The Information Required by Sequence Disclosures Often Has No Practical Utility

At least with respect to amino acid sequences made by chemical synthetic means and which include non-code amino acids, the current rules are both under-inclusive and over-inclusive, rendering the information of little or no practical utility. The current rules do not capture any information which may be meaningfully searched as to the identity of non-coded amino acids, and thus are under-inclusive. By requiring disclosure of amino acid sequences made by chemical synthetic means, and which cannot be made by means of translation of mRNA, the current rules are over-inclusive, and require disclosure of information of little or no practical value or utility.

This is the only art area in which USPTO requires disclosure to be made in a format permitting direct entry of data into a database. While this may serve some useful purpose for nucleotides and naturally expressed peptides and proteins, it serves little or no useful purpose for synthetically made amino acid sequences containing non-coded amino acids, which are conceptually akin to small molecules. The USPTO does not require that small molecules be disclosed in a format permitting direct entry of data into a database; indeed, in many instances it requires considerable effort to even elucidate the structure of disclosed molecules. For example, it is permissible to disclose a compound only by IUPAC nomenclature, without presenting a

chemical structure. Indeed, under current practice even non-conventional nomenclature could be employed, so long as the nomenclature was adequately defined and explained.

It is anomalous that merely because a synthetic compound meets rather arbitrary criteria (at least four amino acids, not branched, no D-amino acids) that it is subject to sequence disclosure requirements, particularly where large numbers of conceptually similar compounds in the very same patent application are excluded under the rules because they contain D-amino acids.

If there is utility in capturing information on nucleotide and naturally expressed peptides and proteins, then the rules should be written to meet this objective. The current rules, which include within their ambit some, but not all, synthetic peptides or proteins (i.e., not made by translation of mRNA) serve no practical utility, particularly given that non-coded amino acids cannot be effectively be searched in existing databases.

The Estimate of Burden is Inaccurate

The estimate of burden, including hours and cost, is unrealistically low, particularly for synthetic amino acid sequences not resulting from translation of mRNA. For example, the USPTO software for sequence listing (PatentIn version 3.5) only permits entry of single letter codes for coded amino acids. This assumes that this source data is readily accessible. For researchers working with nucleotide sequences and translated amino acid sequences, this may be the case. However, researchers developing novel synthetic amino acid constructs do not typically utilize single letter codes, primarily since a single letter code cannot be employed to identify non-coded amino acids. It is typical to either use three letter codes, or alternatively to simply use chemical structures. Preparing a sequence listing thus requires translation from either three letter codes or chemical structures to single letter codes, followed by preparation of the single letter codes in a format suitable for importation into PatentIn. Since many non-coded amino acids are used (including a large number not included in Table 4 of Section 2422 of the MPEP), additional research is required to properly identify individual non-coded amino acids in the features section.

Additionally, because the rules were written primarily with translated amino acid sequences in mind, issues frequently arise which are not adequately addressed by the rules. There have been several instances in my personal experience in which it was apparent that even experts in this area at USPTO were uncertain as how best to comply with rules. Dealing with ambiguity and uncertainty in rules adds significant time to preparation of sequence listing.

I would estimate that preparation of a sequence listing of an average of 60 synthetic amino acid sequences, containing non-code amino acids but still within the ambit of the rules, would require between 4 and 6 hours of paraprofessional time, and between 0.5 and 1 hour of professional time.

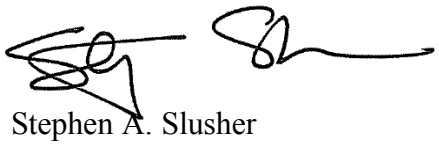
Enhancing the Quality, Utility and Clarity of Information to be Collected

As discussed above, it is not clear why the USPTO (or WIPO) requires that this information be collected, particularly for synthetic amino acid sequences. Even with respect to nucleotide sequences and translated amino acid sequences, it is not clear why USPTO requires that this

information be presented in a specific and rule-driven format when similar requirements are not imposed for other types of data, such as small molecules or amino acid sequences excluded from the rules, such as those sequences containing D-amino acids. With specific reference to amino acid sequences, the information collected is of little or no practical utility except in the case of sequences consisting solely of coded amino acids.

If you have any questions on the foregoing comments, I would be happy to address them at your convenience.

Sincerely yours,



Stephen A. Slusher
Chief Legal Officer

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