STANDARD ST.26

RECOMMENDED STANDARD FOR THE PRESENTATION OF NUCLEOTIDE AND AMINO ACID SEQUENCE LISTINGS USING XML (EXTENSIBLE MARKUP LANGUAGE)

Version ~~1.7~~ 2.0

*Revision approved by the Committee on WIPO Standards (CWS)
at its ~~eleventh~~ thirteenth session on ~~December 8, 2023~~ November 14, 2025*

Editorial Note prepared by the International Bureau

The Thirteenth Session of the Committee on WIPO Standards decided that version 2.0 of ST.26 will enter into force on July 1, 2027 and apply to all patent applications with a filing date on or after that date.

Exceptionally, paragraph 8 of this Standard will apply as from the date of entry into force of version 2.0, independent of the filing date of the patent application concerned. ~~The Eleventh Session of the Committee on WIPO Standards decided that version 1.7 of WIPO Standard ST.26 will enter into force on July 1, 2024. Meanwhile, version 1.6 of WIPO ST.26 should continue to be used~~.

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INTRODUCTION

1. This Standard defines the nucleotide and amino acid sequence disclosures in a patent application required to be included in a sequence listing, the manner in which those disclosures are to be represented, and the Document Type Definition (DTD) for a sequence listing in XML (eXtensible Markup Language). It is recommended that intellectual property offices accept any sequence listing compliant with this Standard filed as part of a patent application or in relation to a patent application.

2. The purpose of this Standard is to:

(a) allow applicants to draw up a single sequence listing in a patent application acceptable for the purposes of both international and national or regional procedures;

(b) enhance the accuracy and quality of presentations of sequences for easier dissemination, benefiting applicants, the public and examiners;

(c) facilitate searching of the sequence data; and

(d) allow sequence data to be exchanged in electronic form and introduced into computerized databases.

DEFINITIONS

3. For the purpose of this Standard, the expression:

(a) "amino acid" means an organic molecule containing an amino group and a carboxyl group. Amino acids intended to be encompassed by this definition, for the purpose of this Standard, include the amino acids listed ~~any amino acid that can be represented using any of the symbols set forth~~ in Annex I, ~~(see~~ Section 3, Table 3 (both D and L stereoisomers) and modifications thereof including but not limited to modifications resulting in a beta-amino acid, a gamma-amino acid, or an N-substituted glycine (see paragraph 29), amino acids containing modified side chains, as well as the modified amino acids listed in Annex I, Section 4, Table 4. ~~Such amino acids include, inter alia, D-amino acids and amino acids containing modified or synthetic side chains.~~ Amino acids will be construed as unmodified L-alpha-amino acids unless further described in the feature table as modified according to paragraph 30. For the purpose of this Standard, a peptide nucleic acid (PNA) residue is not considered an amino acid, but is considered a nucleotide as set forth in paragraph 3(g)(i)(2).

(b) "controlled vocabulary" is the terminology contained in this Standard that must be used when describing the features of a sequence, i.e., annotations of regions or sites of interest as set forth in Annex I.

(c) "enumeration of its residues" means disclosure of a sequence in a patent application by listing, in order, each residue of the sequence, wherein:

(i) the residue is represented by a name, abbreviation, symbol, or structure (e.g., HHHHHHQ or HisHisHisHisHisHisGln); or

(ii) multiple residues are represented by a shorthand formula (e.g., His_6Gln).

(d) "intentionally skipped sequence", also known as an empty sequence, refers to a placeholder to preserve the numbering of sequences in the sequence listing for consistency with the application disclosure, for example, where a sequence is deleted from the disclosure to avoid renumbering of the sequences in both the disclosure and the sequence listing.

(e) "modified amino acid" means any amino acid as described in paragraph 3(a) other than the following L-alpha-amino acids: L-alanine, L-arginine, L-asparagine, L-aspartic acid, L-cysteine, L-glutamine, L-glutamic acid, L-glycine, L-histidine, L-isoleucine, L-leucine, L-lysine, L-methionine, L-phenylalanine, L-proline, L-pyrrolysine, L-serine, L-selenocysteine, L-threonine, L-tryptophan, L-tyrosine, or L-valine.

(f) "modified nucleotide" means any nucleotide as described in paragraph 3(g) other than deoxyadenosine 5'-monophosphate, deoxyguanosine 5'-monophosphate, deoxycytidine 5'-monophosphate, deoxythymidine 5'-monophosphate, adenosine 5'-monophosphate, guanosine 5'-monophosphate, cytidine 5'-monophosphate, or uridine 5'-monophosphate.

(g) "nucleotide" means any nucleotide or nucleotide analogue that can be represented using any of the symbols set forth in Annex I (see Section 1, Table 1) wherein the nucleotide or nucleotide analogue contains:

(i) a backbone moiety selected from:

(1) 2' deoxyribose 5' monophosphate (the backbone moiety of a deoxyribonucleotide) or ribose 5' monophosphate (the backbone moiety of a ribonucleotide); or

(2) an analogue of a 2' deoxyribose 5' monophosphate or ribose 5' monophosphate, which when forming the backbone of a nucleic acid analogue, results in an arrangement of nucleobases that mimics the arrangement of nucleobases in nucleic acids containing a 2' deoxyribose 5' monophosphate or ribose 5' monophosphate backbone, wherein the nucleic acid analogue is capable of base pairing with a complementary nucleic acid; examples of backbone moieties include amino acids as in peptide nucleic acids, glycol molecules as in glycol nucleic acids, threofuranosyl sugar molecules as in threose nucleic acids, morpholine rings and phosphorodiamidate groups as in morpholinos, and cyclohexenyl molecules as in cyclohexenyl nucleic acids.

and

(ii) the backbone moiety is either:

(1) joined to a nucleobase, including a modified or synthetic purine or pyrimidine nucleobase; or

(2) lacking a purine or pyrimidine nucleobase when the nucleotide is part of a nucleotide sequence, referred to as an "AP site" or an "abasic site".

(h) "residue" means any individual nucleotide or amino acid or their respective analogues in a sequence.

(i) "sequence identification number" means a unique number (integer) assigned to each sequence in the sequence listing.

(j) "sequence listing" means a part of the description of the patent application as filed or a document filed subsequently to the application, which includes the disclosed nucleotide and/or amino acid sequence(s), along with any further description, as prescribed by this Standard.

(k) "specifically defined" means any nucleotide other than those represented by the symbol "n" and any amino acid other than those represented by the symbol "X", listed in Annex I (see Section 1, Table 1, and Section 3, Table 3, respectively).

(l) "unknown" nucleotide or amino acid means that a single nucleotide or amino acid is present but its identity is unknown or not disclosed.

(m) "variant sequence" means a nucleotide or amino acid sequence that contains one or more differences with respect to a primary sequence. These differences may include alternative residues (see paragraphs 15 and 27), modified residues (see paragraphs 3(e), 3(f), 3(g), 3(h), 16, and 29), deletions, insertions, and substitutions. See paragraphs 93 to 95.

(n) "free text" is a type of value format for certain qualifiers, presented in the form of a descriptive text phrase or other specified format (as indicated in Annex I). See paragraph 85.

(o) "language-dependent free text" means the free text value of certain qualifiers, which may require translation for international, national or regional procedures. See paragraph 87.

4. For the purpose of this Standard, the word(s):

(a) "may" refers to an optional or permissible approach, but not a requirement.

(b) "must" refers to a requirement of the Standard; disregard of the requirement will result in noncompliance.

(c) "must not" refers to a prohibition of the Standard.

(d) "should" refers to a strongly encouraged approach, but not a requirement.

(e) "should not" refers to a strongly discouraged approach, but not a prohibition.

SCOPE

5. This Standard establishes the requirements for the presentation of nucleotide and amino acid sequence listings of sequences disclosed in patent applications.

6. A sequence listing complying with this Standard (hereinafter sequence listing) contains a general information part and a sequence data part. The sequence listing must be presented as a single file in XML using the Document Type Definition (DTD) presented in Annex II. The purpose of the bibliographic information contained in the general information part is solely for association of the sequence listing to the patent application for which the sequence listing is submitted. The sequence data part is composed of one or more sequence data elements each of which contain information about one sequence. The sequence data elements include various feature keys and subsequent qualifiers based on the International Nucleotide Sequence Database Collaboration (INSDC) and UniProt specifications.

7. For the purpose of this Standard, a sequence for which inclusion in a sequence listing is required is one that is disclosed anywhere in an application by enumeration of its residues and can be represented as:

(a) an unbranched sequence or a linear region of a branched sequence containing ten or more specifically defined nucleotides, wherein adjacent nucleotides are joined by:

(i) a 3' to 5' (or 5' to 3') phosphodiester linkage; or

(ii) any chemical bond that results in an arrangement of adjacent nucleobases that mimics the arrangement of nucleobases in naturally occurring nucleic acids; or

(b) an unbranched sequence or a linear region of a branched sequence containing four or more specifically defined amino acids, wherein the amino acids form a single peptide backbone, i.e., adjacent amino acids are joined by ~~peptide~~ amide bonds formed between a carboxyl group of one amino acid and an amino group of another amino acid.

8. A sequence listing ~~must not~~may include, as a sequence assigned its own sequence identification number, ~~any~~ sequences having fewer than ten specifically defined nucleotides, or fewer than four specifically defined amino acids.

REFERENCES

9. References to the following Standards and resources are of relevance to this Standard:

International Nucleotide Sequence Database Collaboration (INSDC)	http://www.insdc.org/;
International Standard ISO 639-1:2002	Codes for the representation of names of languages - Part 1: Alpha-2 code;
UniProt Consortium	http://www.uniprot.org/;
W3C XML 1.0	http://www.w3.org/;
WIPO Standard ST.2	Standard manner for designating calendar dates by using Gregorian calendar;
WIPO Standard ST.3	Recommended standard on two-letter codes for the representation of states, other entities and intergovernmental organizations;
WIPO Standard ST.16	Recommended standard code for the identification of different kinds of patent documents;
WIPO Standard ST.25	Standard for the presentation of nucleotide and amino acid sequence listings in patent applications.

REPRESENTATION OF SEQUENCES

10. Each sequence encompassed by paragraph 7 must be assigned a separate sequence identification number, including a sequence which is identical to a region of a longer sequence. The sequence identification numbers must begin with number 1, and increase consecutively by integers. Where no sequence is present for a sequence identification number, i.e. an intentionally skipped sequence, "000" must be used in place of a sequence (see paragraph 58). The total number of sequences must be indicated in the sequence listing and must equal the total number of sequence identification numbers, whether followed by a sequence or by "000."

Nucleotide sequences

11. A nucleotide sequence must be represented only by a single strand, in the 5' to 3' direction from left to right, or in the direction from left to right that mimics the 5' to 3' direction. The designations 5' and 3' or any other similar designations must not be included in the sequence. A double-stranded nucleotide sequence disclosed by enumeration of the residues of both strands must be represented as:

(a) a single sequence or as two separate sequences, each assigned its own sequence identification number, where the two separate strands are fully complementary to each other, or

(b) two separate sequences, each assigned its own sequence identification number, where the two strands are not fully complementary to each other.

12. For the purpose of this Standard, the first nucleotide presented in the sequence is residue position number 1. When nucleotide sequences are circular in configuration, applicant must choose the nucleotide in residue position number 1. Numbering is continuous throughout the entire sequence in the 5' to 3' direction, or in the direction that mimics the 5' to 3' direction. The last residue position number must equal the number of nucleotides in the sequence.

13. All nucleotides in a sequence must be represented using the symbols set forth in Annex I (see Section 1, Table 1). Only ~~lower case~~lower-case letters must be used. Any symbol used to represent a nucleotide is the equivalent of only one residue.

14. The symbol "t" will be construed as thymine in DNA and uracil in RNA. Uracil in DNA or thymine in RNA is considered a modified nucleotide and must be further described in the feature table as provided by paragraph 19.

15. Where an ambiguity symbol (representing two or more alternative nucleotides) is appropriate, the most restrictive symbol should be used, as listed in Annex I (section 1, Table 1). For example, if a nucleotide in a given position could be "a" or "g", then "r" should be used, rather than "n". The symbol "n" will be construed as any one of unmodified "a", "c", "g", or "t/u" except where it is used with a further description in the feature table. The symbol "n" must not be used to represent anything other than a nucleotide. A single modified or "unknown" nucleotide may be represented by the symbol "n", together with a further description in the feature table, as provided in paragraphs 16, 17, 21, or 93-96. For representation of sequence variants, i.e., alternatives, deletions, insertions, or substitutions, see paragraphs 93 to 100.

16. Modified nucleotides should be represented in the sequence as the corresponding unmodified nucleotides, i.e., "a", "c", "g" or "t", whenever possible. The "n" symbol must only be used to represent a modified nucleotide when none of the other symbols in Annex I (see Section 1, Table 1) is appropriate. A modified nucleotide with a nucleobase identical to a nucleobase in an unmodified nucleotide listed in Annex I, Section 1, Table 1 must be represented in the sequence as the corresponding unmodified nucleotide. For example, a peptide nucleic acid (PNA) residue with a guanine nucleobase must be represented by a "g" in the sequence and not an "n". ~~Any modified nucleotide in a sequence that cannot otherwise be represented by any other symbol in Annex I (see Section 1, Table 1), i.e., an "other" nucleotide, such as a non-naturally occurring nucleotide, must be represented by the symbol "n".~~ The symbol "n" is the equivalent of only one residue.

17. A modified nucleotide must be further described in the feature table (see paragraph 60 *et seq*.) using the feature key "modified_base" and the mandatory qualifier "mod_base" in conjunction with a single abbreviation from Annex I (see Section 2, Table 2) as the qualifier value; if the abbreviation is "OTHER", the complete unabbreviated name of the modified nucleotide must be provided as the value in a "note" qualifier. For a listing of alternative modified nucleotides, the qualifier value "OTHER" may be used in conjunction with a further "note" qualifier (see paragraphs 97 and 98). The abbreviations (or full names) provided in Annex I (see Section 2, Table 2) referred to above must not be used in the sequence itself.

18. A nucleotide sequence including one or more regions of consecutive modified nucleotides that share the same backbone moiety (see paragraph 3(g)(i)(2)), must be further described in the feature table as provided by paragraph 17. The modified nucleotides of each such region may be jointly described in a single INSDFeature element as provided by paragraph 22. The most restrictive unabbreviated chemical name that encompasses all of the modified nucleotides in the range or a list of the chemical names of all the nucleotides in the range must be provided as the value in the "note" qualifier. For example, a glycol nucleic acid sequence containing "a", "c", "g", or "t" nucleobases may be described in the "note" qualifier as "2,3-dihydroxypropyl nucleosides." Alternatively, the same sequence may be described in the "note" qualifier as "2,3-dihydroxypropyladenine, 2,3-dihydroxypropylthymine, 2,3-dihydroxypropylguanine, or 2,3-dihydroxypropylcytosine." Where an individual modified nucleotide in the region includes an additional modification, then the modified nucleotide must also be further described in the feature table as provided in paragraph 17.

19. Uracil in DNA or thymine in RNA are considered modified nucleotides and must be represented in the sequence as "t" and be further described in the feature table using the feature key "modified_base", the qualifier "mod_base" with "OTHER" as the qualifier value and the qualifier "note" with "uracil" or "thymine", respectively, as the qualifier value.

20. The following examples illustrate the representation of modified nucleotides according to paragraphs 16 to 18 above:

Example 1: Modified nucleotide using an abbreviation from Annex I (see Section 2, Table 2)

```
<INSDFeature>
    <INSDFeature_key>modified_base</INSDFeature_key>
    <INSDFeature_location>15</INSDFeature_location>
    <INSDFeature_quals>
        <INSDQualifier>
            <INSDQualifier_name>mod_base</INSDQualifier_name>
            <INSDQualifier_value>i</INSDQualifier_value>
        </INSDQualifier>
    </INSDFeature_quals>
</INSDFeature>
```

Example 2: Modified nucleotide using “OTHER” from Annex I (see Section 2, Table 2)

```
<INSDFeature>
    <INSDFeature_key>modified_base</INSDFeature_key>
    <INSDFeature_location>4</INSDFeature_location>
    <INSDFeature_quals>
        <INSDQualifier>
            <INSDQualifier_name>mod_base</INSDQualifier_name>
            <INSDQualifier_value>OTHER</INSDQualifier_value>
        </INSDQualifier>
        <INSDQualifier>
            <INSDQualifier_name>note</INSDQualifier_name>
            <INSDQualifier_value>xanthine</INSDQualifier_value>
        </INSDQualifier>
    </INSDFeature_quals>
</INSDFeature>
```

Example 3: A nucleotide sequence composed of modified nucleotides encompassed by paragraph 3(g)(i)(2) with two individual nucleotides that include a further modification

```
<INSDFeature>
    <INSDFeature_key>modified_base</INSDFeature_key>
    <INSDFeature_location>1..954</INSDFeature_location>
    <INSDFeature_quals>
        <INSDQualifier>
            <INSDQualifier_name>mod_base</INSDQualifier_name>
            <INSDQualifier_value>OTHER</INSDQualifier_value>
        </INSDQualifier>
        <INSDQualifier>
            <INSDQualifier_name>note</INSDQualifier_name>
            <INSDQualifier_value>2,3-dihydroxypropyl nucleosides</INSDQualifier_value>
        </INSDQualifier>
    </INSDFeature_quals>
</INSDFeature>
<INSDFeature>
    <INSDFeature_key>modified_base</INSDFeature_key>
    <INSDFeature_location>439</INSDFeature_location>
    <INSDFeature_quals>
        <INSDQualifier>
            <INSDQualifier_name>mod_base</INSDQualifier_name>
            <INSDQualifier_value>i</INSDQualifier_value>
        </INSDQualifier>
    </INSDFeature_quals>
</INSDFeature>
<INSDFeature>
    <INSDFeature_key>modified_base</INSDFeature_key>
    <INSDFeature_location>684</INSDFeature_location>
    <INSDFeature_quals>
        <INSDQualifier>
            <INSDQualifier_name>mod_base</INSDQualifier_name>
            <INSDQualifier_value>OTHER</INSDQualifier_value>
        </INSDQualifier>
        <INSDQualifier>
            <INSDQualifier_name>note</INSDQualifier_name>
            <INSDQualifier_value>xanthine</INSDQualifier_value>
        </INSDQualifier>
    </INSDFeature_quals>
```

```
</INSDFeature>
```

21. Any “unknown” nucleotide must be represented by the symbol “n” in the sequence. An “unknown” nucleotide should be further described in the feature table (see paragraph 60 *et seq.*) using the feature key “unsure”. The symbol “n” is the equivalent of only one residue.

22. A region containing a known number of contiguous nucleotide ~~“a”, “c”, “g”, “t”, or “n”~~ residues for which the same description applies may be jointly described using a single INSDFeature element with the syntax “x..y” as the location descriptor in the element `INSDFeature_location` (see paragraphs 64 to 71). For representation of sequence variants, i.e., alternatives, deletions, insertions or substitutions, see paragraphs 93 to 100.

23. The following example illustrates the representation of a region of modified nucleotides for which the same description applies, according to paragraph 22 above:

```
<INSDFeature>
        <INSDFeature_key>modified_base</INSDFeature_key>
        <INSDFeature_location>358..485</INSDFeature_location>
        <INSDFeature_quals>
                <INSDQualifier>
                        <INSDQualifier_name>mod_base</INSDQualifier_name>
                        <INSDQualifier_value>OTHER</INSDQualifier_value>
                </INSDQualifier>
                <INSDQualifier>
                        <INSDQualifier_name>note</INSDQualifier_name>
                        <INSDQualifier_value>isoguanine</INSDQualifier_value>
                </INSDQualifier>
        </INSDFeature_quals>
</INSDFeature>
```

Amino acid sequences

24. The amino acids in an amino acid sequence must be represented in the amino to carboxy direction from left to right. The amino and carboxy groups must not be represented in the sequence.

25. For the purpose of this Standard, the first amino acid in the sequence is residue position number 1, including amino acids preceding the mature protein, for example, pre-sequences, pro-sequences, pre-pro-sequences and signal sequences. When an amino acid sequence is circular in configuration and the ring consists solely of amino acid residues linked by ~~peptide~~ amide bonds, i.e., the sequence has no amino and carboxy termini, applicant must choose the amino acid in residue position number 1. Numbering is continuous through the entire sequence in the amino to carboxy direction.

26. All amino acids in a sequence must be represented using the symbols set forth in Annex I (see Section 3, Table 3). Only ~~upper case~~upper-case letters must be used. Any symbol used to represent an amino acid is the equivalent of only one residue.

27. Where an ambiguity symbol (representing two or more amino acids in the alternative) is appropriate, the most restrictive symbol should be used, as listed in Annex I (Section 3, Table 3). For example, if an amino acid in a given position could be aspartic acid or asparagine, the symbol “B” should be used, rather than “X”. The symbol “X” will be construed as any one of the unmodified L-alpha-amino acids “A”, “R”, “N”, “D”, “C”, “Q”, “E”, “G”, “H”, “I”, “L”, “K”, “M”, “F”, “P”, “O”, “S”, “U”, “T”, “W”, “Y”, or “V”, except where it is used with a further description in the feature table. The symbol “X” must not be used to represent anything other than an amino acid. A single modified or “unknown” amino acid may be represented by the symbol “X”, when none of the other symbols in Annex I (see Section 3, Table 3) is appropriate, together with a further description in the feature table, e.g., as provided by paragraphs 29, 30, 32, or 93-98. For representation of sequence variants, i.e., alternatives, deletions, insertions, or substitutions, see paragraphs 93 to 100.

28. Disclosed amino acid sequences separated by internal terminator symbols, represented for example by “Ter” or asterisk “*” or period “.” or a blank space, must be included as separate sequences for each amino acid sequence that contains at least four specifically defined amino acids and is encompassed by paragraph 7. Each such separate sequence must be assigned its own sequence identification number. Terminator symbols and spaces must not be included in sequences in a sequence listing (see paragraph 57).

29. Modified amino acids~~, including D-amino acids,~~ should be represented in the sequence ~~as~~ by the corresponding unmodified amino ~~acids~~ acid symbol whenever possible. The “X” symbol must only be used to represent a modified amino acid when none of the other symbols in Annex I (see Section 3, Table 3) is suitable. ~~Any modified amino acid in a sequence that cannot otherwise be represented by any other symbol in Annex I (see Section 3, Table 3), i.e., an “other” amino acid, must be represented by “X”.~~ A modified amino acid having a single carbon-containing side chain that is identical to the side chain in a L-alpha-amino acid listed in Annex I, Section 3, Table 3, and that is located on:

(a) the amino nitrogen of the residue instead of the alpha carbon (e.g., an N-substituted glycine); or

(b) any of the backbone atoms of an amino acid having an extended carbon backbone, such as beta amino acids or gamma amino acids; or

(c) the alpha carbon but as the D-stereoisomer

must be represented in the sequence by the corresponding unmodified amino acid symbol, i.e., the amino acid in Annex I, Section 3, Table 3 having the identical side chain. For example, an N-substituted glycine residue with an isobutyl group attached to the amino nitrogen must be represented by "L" in the sequence, and not "G" or "X", because the L-alpha-amino acid leucine listed in Annex I, Section 3, Table 3 has an identical isobutyl side chain. A modified amino acid having multiple carbon-containing side chains should be represented by a corresponding unmodified amino acid or as an "other" amino acid (i.e., "X"), as most appropriate. The symbol "X" is the equivalent of only one residue.

30. A modified amino acid must be further described in the feature table (see paragraph 60 *et seq.*). Where applicable, the feature keys "CARBOHYD" or "LIPID" should be used together with the mandatory qualifier "note". The feature key "MOD_RES" should be used for other post-translationally modified amino acids together with the mandatory qualifier "note". A modified amino acid for which "CARBOHYD", "LIPID" or "MOD_RES" is not appropriate, i.e., a non-post-translationally modified amino acid, should be described using ~~otherwise~~ the feature key "SITE" together with the mandatory qualifier "note" ~~should be used~~. The value for the qualifier "note" must either be an abbreviation set forth in Annex I (see Section 4, Table 4), or the complete, unabbreviated name of the modified amino acid. The abbreviations set forth in Table 4 referred to above or the complete, unabbreviated names must not be used in the sequence itself.

31. The following examples illustrate the representation of modified amino acids according to paragraph 30 above:

Example 1: Post-translationally modified amino acid

```
<INSDFeature>
    <INSDFeature_key>MOD_RES</INSDFeature_key>
    <INSDFeature_location>3</INSDFeature_location>
    <INSDFeature_quals>
        <INSDQualifier>
            <INSDQualifier_name>note</INSDQualifier_name>
            <INSDQualifier_value>3Hyp</INSDQualifier_value>
        </INSDQualifier>
    </INSDFeature_quals>
</INSDFeature>
```

Example 2: Non post-translationally modified amino acid

```
<INSDFeature>
    <INSDFeature_key>SITE</INSDFeature_key>
    <INSDFeature_location>3</INSDFeature_location>
    <INSDFeature_quals>
        <INSDQualifier>
            <INSDQualifier_name>note</INSDQualifier_name>
            <INSDQualifier_value>Orn</INSDQualifier_value>
        </INSDQualifier>
    </INSDFeature_quals>
</INSDFeature>
```

Example 3: D-amino acid

```
<INSDFeature>
    <INSDFeature_key>SITE</INSDFeature_key>
    <INSDFeature_location>9</INSDFeature_location>
    <INSDFeature_quals>
        <INSDQualifier>
            <INSDQualifier_name>note</INSDQualifier_name>
            <INSDQualifier_value>D-Arginine</INSDQualifier_value>
        </INSDQualifier>
    </INSDFeature_quals>
</INSDFeature>
```

32. Any "unknown" amino acid must be represented by the symbol "X" in the sequence. An "unknown" amino acid designated as "X" must be further described in the feature table (see paragraph 60 *et seq.*) using the feature key "UNSURE" and optionally the qualifier "note." The symbol "X" is the equivalent of only one residue.

33. The following example illustrates the representation of an "unknown" amino acid according to paragraph 32 above:

```
<INSDFeature>
    <INSDFeature_key>UNSURE</INSDFeature_key>
    <INSDFeature_location>3</INSDFeature_location>
    <INSDFeature_quals>
        <INSDQualifier>
            <INSDQualifier_name>note</INSDQualifier_name>
            <INSDQualifier_value>A or V</INSDQualifier_value>
        </INSDQualifier>
    </INSDFeature_quals>
</INSDFeature>
```

34. A region containing a known number of contiguous amino acid ~~"X"~~ residues for which the same description applies may be jointly described using the syntax "x..y" as the location descriptor in the element INSDFeature_location (see paragraphs 64 to 710). For representation of sequence variants, i.e., alternatives, deletions, insertions, or substitutions, see paragraphs 93 to 100.

Presentation of special situations

35. A sequence disclosed by enumeration of its residues that is constructed as a single continuous sequence from one or more non-contiguous segments of a larger sequence or of segments from different sequences must be included in the sequence listing and assigned its own sequence identification number.

36. A sequence that contains regions of specifically defined residues separated by one or more regions of contiguous "n" or "X" residues (see paragraphs 15 and 27, respectively), wherein the exact number of "n" or "X" residues in each region is disclosed, must be included in the sequence listing as one sequence and assigned its own sequence identification number.

37. A sequence that contains regions of specifically defined residues separated by one or more gaps of an unknown or undisclosed number of residues must not be represented in the sequence listing as a single sequence. Each region of specifically defined residues that is encompassed by paragraph 7 must be included in the sequence listing as a separate sequence and assigned its own sequence identification number.

STRUCTURE OF THE SEQUENCE LISTING IN XML

38. In accordance with paragraph 6 above, an XML instance of a sequence listing file according to this Standard is composed of:

(a) a general information part, which contains information concerning the patent application to which the sequence listing is directed; and

(b) a sequence data part, which contains one or more sequence data elements, each of which, in turn, contain information about one sequence.

An example of a sequence listing is provided in Annex III.

39. The sequence listing must be presented in XML 1.0 using the DTD presented in the Annex II "Document Type Definition (DTD) for Sequence Listing".

(a) The first line of the XML instance must contain the XML declaration:

```
<?xml version="1.0" encoding="UTF-8"?>.
```

(b) The second line of the XML instance must contain a document type (DOCTYPE) declaration:

```
<!DOCTYPE ST26SequenceListing PUBLIC "-//WIPO//DTD Sequence Listing 1.3//EN"
"ST26SequenceListing_V1_3.dtd">.
```

40. The entire electronic sequence listing must be contained within one file. The file must be encoded using Unicode UTF-8, with the following restrictions:

(a) the information contained in the elements `ApplicantName`, `InventorName` and `InventionTitle` of the general information part, and the `NonEnglishQualifier_value` of the sequence data part, may be composed of any valid Unicode characters indicated in the XML 1.0 specification except the Unicode Control code points 0000-001F and 007F-009F. The reserved characters ", &, ', <, and > (Unicode code points 0022, 0026, 0027, 003C and 003E respectively), must be replaced as set forth in paragraph 41; and

(b) the information contained in all other elements and attributes of the general information part and in all other elements and attributes of the sequence data part must be composed of printable characters (including the space character) from the Unicode Basic Latin code table (i.e., limited to Unicode code points 0020 through 007E – see Annex IV). The reserved characters “, &, ‘, <, and > (Unicode code points 0022, 0026, 0027, 003C and 003E respectively), must be replaced as set forth in paragraph 41.

41. In an XML instance of a sequence listing, numeric character references[1] must not be used and the following reserved characters must be replaced by the corresponding predefined entities when used in a value of an attribute or content of an element:

Reserved Character	Predefined Entities
<	<
>	>
&	&
“	"
'	'

See paragraph 71 for an example. The only character entity references permitted are the predefined entities set forth in this paragraph.

42. All mandatory elements must be populated (except as provided for in paragraph 58 for an intentionally skipped sequence). Optional elements for which content is not available ~~should~~ must not appear in the XML instance (except as provided for in paragraph 97 for representation of a deletion in a sequence in the value for the qualifier “replace”).

Root element

43. The root element of an XML instance according to this Standard is the element `ST26SequenceListing`, having the following attributes:

Attribute	Description	Mandatory/Optional
`dtdVersion`	Version of the DTD used to create this file in the format “V#_#”, e.g., “V1_3”.	Mandatory
`fileName`	Name of the sequence listing file.	Optional
`softwareName`	Name of the software that generated this file.	Optional
`softwareVersion`	Version of the software that generated this file.	Optional
`productionDate`	Date of production of the sequence listing file (format “CCYY-MM-DD”).	Optional
`originalFreeTextLanguageCode`	The language code (see reference in paragraph 9 to ISO 639-1:2002) for the single original language in which the language-dependent free text qualifiers were prepared.	Optional
`nonEnglishFreeTextLanguageCode`	The language code (see reference in paragraph 9 to ISO 639-1:2002) for the `NonEnglishQualifier_value` elements	Mandatory when a `NonEnglishQualifier_value` element is present in the sequence listing

44. The following example illustrates the root element `ST26SequenceListing`, and its attributes, of an XML instance as per paragraph 43 above:

[1] A numeric character reference refers to a character by its Universal Character Set/Unicode code point, and uses the format: “&#nnnn;” or “&#xhhhh;”, where “nnnn” is the code point in decimal form, and “hhhh” is the code point in hexadecimal form.

```
<ST26SequenceListing dtdVersion="V1_3" fileName="US11-405455-SEQL.xml"
softwareName="WIPO Sequence" softwareVersion="1.0" productionDate="2022-05-10"
originalFreeTextLanguageCode="de" nonEnglishFreeTextLanguageCode="fr">
  {...}*
</ST26SequenceListing>

*{...} represents the general information part and the sequence data part that have
not been included in this example.
```

General information part

45. The elements of the general information part relate to patent application information, as follows:

Element	Description	Mandatory/ Optional
`ApplicationIdentification` The `ApplicationIdentification` is composed of:	The application identification for which the sequence listing is submitted	Mandatory when a sequence listing is furnished at any time following the assignment of the application number
`IPOfficeCode`	ST.3 Code of the office of filing	Mandatory
`ApplicationNumberText`	The application number as provided by the office of filing (e.g., PCT/IB2013/099999).	Mandatory
`FilingDate`	The date of filing of the patent application for which the sequence listing is submitted (ST.2 format "CCYY-MM-DD", using a 4-digit calendar year, a 2-digit calendar month and a 2-digit day within the calendar month, e.g., 2015-01-31)	Mandatory when a sequence listing is furnished at any time following the assignment of a filing date
`ApplicantFileReference`	A single unique identifier assigned by applicant to identify a particular application, typed in the characters as set forth in paragraph 40 (b)	Mandatory when a sequence listing is furnished at any time prior to assignment of the application number; otherwise, Optional
`EarliestPriorityApplicationIdentification`	The identification of the earliest priority application (also contains `IPOfficeCode`, `ApplicationNumberText` and `FilingDate`, see `ApplicationIdentification` above)	Mandatory where priority is claimed
`ApplicantName`	Name of the first mentioned applicant typed in the characters as set forth in paragraph 40 (a). This element includes the mandatory attribute `languageCode` as set forth in paragraph 47.	Mandatory

Element	Description	Mandatory/ Optional
ApplicantNameLatin	Where ApplicantName is typed in characters other than those as set forth in paragraph 40 (b), a translation or transliteration of the name of the first mentioned applicant must also be typed in characters as set forth in paragraph 40 (b)	Mandatory where ApplicantName contains non-Latin characters
InventorName	Name of the first mentioned inventor typed in the characters as set forth in paragraph 40 (a). This element includes the mandatory attribute languageCode as set forth in paragraph 47.	Optional
InventorNameLatin	Where InventorName is typed in characters other than those as set forth in paragraph 40 (b), a translation or transliteration of the first mentioned inventor may also be typed in characters as set forth in paragraph 40 (b)	Optional
InventionTitle	Title of the invention typed in the characters as set forth in paragraph 40 (a) in the language of filing. A translation of the title of the invention into additional languages may be typed in the characters as set forth in paragraph 40 (a) using additional InventionTitle elements. This element includes the mandatory attribute languageCode as set forth in paragraph 48. The title of invention should be between two to seven words.	Mandatory in the language of filing. Optional for additional languages.
SequenceTotalQuantity	The total number of all sequences in the sequence listing including intentionally skipped sequences (also known as empty sequences) (see paragraph 10).	Mandatory

46. The following examples illustrate the presentation of the general information part of the sequence listing as per paragraph 45 above:

Example 1: Sequence listing filed prior to assignment of the application identification and filing date

```
<?xml version="1.0" encoding="UTF-8"?>
<!DOCTYPE ST26SequenceListing PUBLIC "-//WIPO//DTD Sequence Listing 1.3//EN"
"ST26SequenceListing_V1_3.dtd">
<ST26SequenceListing dtdVersion="V1_3" fileName="Invention_SEQL.xml"
softwareName="WIPO Sequence" softwareVersion="1.0" productionDate="2022-05-10"
originalFreeTextLanguageCode="en" nonEnglishFreeTextLanguageCode="ja">
    <ApplicantFileReference>AB123</ApplicantFileReference>
    <EarliestPriorityApplicationIdentification>
        <IPOfficeCode>IB</IPOfficeCode>
        <ApplicationNumberText>PCT/IB2013/099999</ApplicationNumberText>
         <FilingDate>2014-07-10</FilingDate>
    </EarliestPriorityApplicationIdentification>
    <ApplicantName languageCode="en">GENOS Co., Inc.</ApplicantName>
    <InventorName languageCode="en">Keiko Nakamura</InventorName>
    <InventionTitle languageCode="en">SIGNAL RECOGNITION PARTICLE RNA AND
PROTEINS</InventionTitle>
    <SequenceTotalQuantity>9</SequenceTotalQuantity>
    <SequenceData sequenceIDNumber="1"> {...}* </SequenceData>
    <SequenceData sequenceIDNumber="2"> {...} </SequenceData>
```

```
    <SequenceData sequenceIDNumber="3"> {...} </SequenceData>
    <SequenceData sequenceIDNumber="4"> {...} </SequenceData>
    <SequenceData sequenceIDNumber="5"> {...} </SequenceData>
    <SequenceData sequenceIDNumber="6"> {...} </SequenceData>
    <SequenceData sequenceIDNumber="7"> {...} </SequenceData>
    <SequenceData sequenceIDNumber="8"> {...} </SequenceData>
    <SequenceData sequenceIDNumber="9"> {...} </SequenceData>
</ST26SequenceListing>

*{...} represents relevant information for each sequence that has not been included in
this example.
```

Example 2: Sequence listing filed after assignment of the application identification and filing date

```
<?xml version="1.0" encoding="UTF-8"?>
<!DOCTYPE ST26SequenceListing PUBLIC WIPO//DTD Sequence Listing 1.3//EN"
"ST26SequenceListing_V1_3.dtd">
<ST26SequenceListing dtdVersion="1_3" fileName="Invention_SEQL.xml" softwareName="WIPO
Sequence" softwareVersion="1.0" productionDate="2022-05-10"
originalFreeTextLanguageCode="en" nonEnglishFreeTextLanguageCode="ja">
     <ApplicationIdentification>
        <IPOfficeCode>US</IPOfficeCode>
        <ApplicationNumberText>14/999,999</ApplicationNumberText>
        <FilingDate>2015-01-05</FilingDate>
    </ApplicationIdentification>
    <ApplicantFileReference>AB123</ApplicantFileReference>
    <EarliestPriorityApplicationIdentification>
        <IPOfficeCode>IB</IPOfficeCode>
        <ApplicationNumberText>PCT/IB2014/099999</ApplicationNumberText>
        <FilingDate>2014-07-10</FilingDate>
    </EarliestPriorityApplicationIdentification>
    <ApplicantName languageCode="en">GENOS Co., Inc.</ApplicantName>
    <InventorName languageCode="en">Keiko Nakamura</InventorName>
    <InventionTitle languageCode="en">SIGNAL RECOGNITION PARTICLE RNA AND
PROTEINS</InventionTitle>
    <SequenceTotalQuantity>9</SequenceTotalQuantity>
    <SequenceData sequenceIDNumber="1"> {...}* </SequenceData>
    <SequenceData sequenceIDNumber="2"> {...} </SequenceData>
    <SequenceData sequenceIDNumber="3"> {...} </SequenceData>
    <SequenceData sequenceIDNumber="4"> {...} </SequenceData>
    <SequenceData sequenceIDNumber="5"> {...} </SequenceData>
    <SequenceData sequenceIDNumber="6"> {...} </SequenceData>
    <SequenceData sequenceIDNumber="7"> {...} </SequenceData>
    <SequenceData sequenceIDNumber="8"> {...} </SequenceData>
    <SequenceData sequenceIDNumber="9"> {...} </SequenceData>
</ST26SequenceListing>*
{...} represents relevant information for each sequence that has not been included in
this example.
```

47. The name of the applicant and, optionally, the name of the inventor must be indicated in the element `ApplicantName` and `InventorName`, respectively, as they are generally referred to in the language in which the application is filed. The appropriate language code (see reference in paragraph 9 to ISO 639-1:2002) must be indicated in the `languageCode` attribute for each element. Where the applicant name indicated contains characters other than those of the Latin alphabet as set forth in paragraph 40 (b), a transliteration or translation of the applicant name must also be indicated in characters of the Latin alphabet in the element `ApplicantNameLatin`. Where the inventor name indicated contains characters other than those of the Latin alphabet, a transliteration or a translation of the inventor name may also be indicated in characters of the Latin alphabet in the element `InventorNameLatin`.

48. The title of the invention must be indicated in the element `InventionTitle` in the language of filing and may also be indicated in additional languages using multiple `InventionTitle` elements (see table in paragraph 45). The appropriate language code (see reference in paragraph 9 to ISO 639-1:2002) must be indicated in the `languageCode` attribute of the element.

49. The following example illustrates the presentation of names and title of the invention as per paragraphs 47 and 48 above:

Example: Applicant name and inventor name are each presented in Japanese and Latin characters and the title of the invention is presented in Japanese, English and French

```
<ApplicantName languageCode="ja">出願製薬株式会社</ApplicantName>
<ApplicantNameLatin>Shutsugan Pharmaceuticals Kabushiki Kaisha</ApplicantNameLatin>
<InventorName languageCode="ja">特許 太郎</InventorName>
<InventorNameLatin>Taro Tokkyo</InventorNameLatin>
<InventionTitle languageCode="ja">efg タンパク質をコードするマウス abcd-1 遺伝子
</InventionTitle>
<InventionTitle languageCode="en">Mus musculus abcd-1 gene for efg
protein</InventionTitle>
<InventionTitle languageCode="fr">Gène abcd-1 de Mus musculus pour protéine
efg</InventionTitle>
```

Sequence data part

50. The sequence data part must be composed of one or more `SequenceData` elements, each element containing information about one sequence.

51. Each `SequenceData` element must have a mandatory attribute `sequenceIDNumber`, in which the sequence identification number (see paragraph 10) for each sequence is contained. For example:

```
<SequenceData sequenceIDNumber="1">
```

52. The `SequenceData` element must contain a dependent element `INSDSeq`, consisting of further dependent elements as follows:

Element	Description	Mandatory/Not Included	
		Sequences	Intentionally Skipped Sequences
`INSDSeq_length`	Length of the sequence	Mandatory	Mandatory with no value
`INSDSeq_moltype`	Molecule type	Mandatory	Mandatory with no value
`INSDSeq_division`	Indication that a sequence is related to a patent application	Mandatory with the value “PAT”	Mandatory with no value
`INSDSeq_feature-table`	List of annotations of the sequence	Mandatory	Must NOT be included
`INSDSeq_sequence`	Sequence	Mandatory	Mandatory with the value “000”

53. The element `INSDSeq_length` must disclose the number of nucleotides or amino acids of the sequence contained in the `INSDSeq_sequence` element. For example:

```
<INSDSeq_length>8</INSDSeq_length>
```

54. The element `INSDSeq_moltype` must disclose the type of molecule that is being represented. For nucleotide sequences, including nucleotide analogue sequences, the molecule type must be indicated as DNA or RNA. For amino acid sequences, the molecule type must be indicated as AA. (This element is distinct from the qualifier “mol_type” discussed in paragraphs 55 and 84). For example:

```
<INSDSeq_moltype>AA</INSDSeq_moltype>
```

55. For a nucleotide sequence that contains both DNA and RNA segments of one or more nucleotides, the molecule type must be indicated as DNA. The combined DNA/RNA molecule must be further described in the feature table, using the feature key “source” and the mandatory qualifier “organism” with the value “synthetic construct” and the mandatory qualifier “mol_type” with the value “other DNA”. Each DNA and RNA segment of the combined DNA/RNA molecule must be further described with the feature key “misc_feature” and the qualifier “note”, which indicates whether the segment is DNA or RNA.

56. The following example illustrates the description of a nucleotide sequence containing both DNA and RNA segments as per paragraph 55 above:

```
<INSDSeq>
    <INSDSeq_length>120</INSDSeq_length>
    <INSDSeq_moltype>DNA</INSDSeq_moltype>
    <INSDSeq_division>PAT</INSDSeq_division>
    <INSDSeq_feature-table>
        <INSDFeature>
            <INSDFeature_key>source</INSDFeature_key>
            <INSDFeature_location>1..120</INSDFeature_location>
            <INSDFeature_quals>
                <INSDQualifier>
                    <INSDQualifier_name>organism</INSDQualifier_name>
                    <INSDQualifier_value>synthetic construct</INSDQualifier_value>
                </INSDQualifier>
                <INSDQualifier>
                    <INSDQualifier_name>mol_type</INSDQualifier_name>
                    <INSDQualifier_value>other DNA</INSDQualifier_value>
                </INSDQualifier>
            </INSDFeature_quals>
        </INSDFeature>
        <INSDFeature>
            <INSDFeature_key>misc_feature</INSDFeature_key>
            <INSDFeature_location>1..60</INSDFeature_location>
            <INSDFeature_quals>
                <INSDQualifier>
                    <INSDQualifier_name>note</INSDQualifier_name>
                    <INSDQualifier_value>DNA</INSDQualifier_value>
                </INSDQualifier>
            </INSDFeature_quals>
        </INSDFeature>
        <INSDFeature>
            <INSDFeature_key>misc_feature</INSDFeature_key>
            <INSDFeature_location>61..120</INSDFeature_location>
            <INSDFeature_quals>
                <INSDQualifier>
                    <INSDQualifier_name>note</INSDQualifier_name>
                    <INSDQualifier_value>RNA</INSDQualifier_value>
                </INSDQualifier>
            </INSDFeature_quals>
        </INSDFeature>
    </INSDSeq_feature-table>
<INSDSeq_sequence>cgacccacgcgtccgaggaaccaaccatcacgtttgaggacttcgtgaaggaattggataatacccgt
ccctaccaaaatggcgagcgccgactcattgctcctcgtaccgtcgagcggc</INSDSeq_sequence>
</INSDSeq>
```

57. The element `INSDSeq_sequence` must disclose the sequence. Only the appropriate symbols set forth in Annex I (see Section 1, Table 1 and Section 3, Table 3) must be included in the sequence. The sequence must not include numbers, punctuation or whitespace characters.

58. An intentionally skipped sequence must be included in the sequence listing and represented as follows:

(a) the element `SequenceData` and its attribute `sequenceIDNumber`, with the sequence identification number of the skipped sequence provided as the value;

(b) the elements `INSDSeq_length`, `INSDSeq_moltype`, `INSDSeq_division`, present but with no value provided;

(c) the element `INSDSeq_feature-table` must not be included; and

(d) the element `INSDSeq_sequence` with the string “000” as the value.

59. The following example illustrates the representation of an intentionally skipped sequence as per paragraph 58 above:

```
<SequenceData sequenceIDNumber="3">
    <INSDSeq>
```

```
            <INSDSeq_length/>
            <INSDSeq_moltype/>
            <INSDSeq_division/>
            <INSDSeq_sequence>000</INSDSeq_sequence>
        </INSDSeq>
    </SequenceData>
```

Feature table

60. The feature table contains information on the location and roles of various regions within a particular sequence. A feature table is required for every sequence, except for any intentionally skipped sequence, in which case it must not be included. The feature table is contained in the element `INSDSeq_feature-table`, which consists of one or more `INSDFeature` elements.

61. Each `INSDFeature` element describes one feature, and consists of dependent elements as follows:

Element	Description	Mandatory/Optional
`INSDFeature_key`	A word or abbreviation indicating a feature	Mandatory
`INSDFeature_location`	Region of the sequence which corresponds to the feature	Mandatory
`INSDFeature_quals`	Qualifier containing auxiliary information about a feature	Mandatory where the feature key requires one or more qualifiers, e.g., source; otherwise, Optional

Feature keys

62. Annex I contains an exclusive listing of feature keys that must be used under this Standard, along with an exclusive listing of associated qualifiers and an indication as to whether those qualifiers are mandatory or optional. Section 5 of Annex I provides the exclusive listing of feature keys for nucleotide sequences and Section 7 provides the exclusive listing of feature keys for amino acid sequences.

Mandatory feature keys

63. The “source” feature key is mandatory for all nucleotide sequences and for all amino acid sequences, except for any intentionally skipped sequence. Each sequence must have a single “source” feature key spanning the entire sequence. Where a sequence originates from multiple sources, those sources may be further described in the feature table, using the feature key “misc_feature” and the qualifier “note” for nucleotide sequences, and the feature key “REGION” and the qualifier “note” for amino acid sequences.

Feature location

64. The mandatory element `INSDFeature_location` must contain at least one location descriptor, which defines a site or a region corresponding to a feature of the sequence in the `INSDSeq_sequence` element. Amino acid sequences must contain one and only one location descriptor in the mandatory `INSDFeature_location` element. Nucleotide sequences may have more than one location descriptor in the mandatory `INSDFeature_location` element when used in conjunction with one or more location operator(s) (see paragraphs 67 to 70).

65. The location descriptor can be a single residue number, a region delimiting a contiguous span of residue numbers, or a site or region that extends beyond the specified residue or span of residues. The location descriptor must not include numbering for residues beyond the range of the sequence in the `INSDSeq_sequence` element. For nucleotide sequences only, a location descriptor can be a site between two adjacent residue numbers. Multiple location descriptors must be used in conjunction with a location operator when a feature corresponds to discontinuous sites or regions of a nucleotide sequence (see paragraphs 67 to 70).

66. The syntax for each type of location descriptor is indicated in the table below, where x and y are residue numbers, indicated as positive integers, not greater than the length of the sequence in the `INSDSeq_sequence` element, and x is less than y.

(a) Location descriptors for nucleotide and amino acid sequences:

Location descriptor type	Syntax	Description
Single residue number	`x`	Points to a single residue in the sequence.

Location descriptor type	Syntax	Description
Residue numbers delimitating a sequence span	`x..y`	Points to a continuous range of residues bounded by and including the starting and ending residues.

Residues before the first or beyond the last specified residue number	`<x`
	`>x`
	`<x..y`
	`x..>y`
	`<x..>y`
		Points to a region including a specified residue or span of residues and extending beyond a specified residue. The '<' and '>' symbols may be used with a single residue or the starting and ending residue numbers of a span of residues to indicate that a feature extends beyond the specified residue number.

(b) Location descriptors for nucleotide sequences only:

Location descriptor type	Syntax	Description
A site between two adjoining nucleotides	`x^y`	Points to a site between two adjoining nucleotides, e.g., endonucleolytic cleavage site. The position numbers for the adjacent nucleotides are separated by a carat (^). The permitted formats for this descriptor are x^x+1 (for example 55^56), or, for circular nucleotides, x^1, where “x” is the full length of the molecule, i.e. 1000^1 for circular molecule with length 1000.

(c) Location descriptors for amino acid sequences only:

Location descriptor type	Syntax	Description
Residue numbers joined by an intrachain cross-link	`x..y`	Points to amino acids joined by an intrachain linkage when used with a feature that indicates an intrachain cross-link, such as “CROSSLNK” or “DISULFID”.

67. The INSDFeature_location element of nucleotide sequences may contain one or more location operators. A location operator is a prefix to either one location descriptor or a combination of location descriptors corresponding to a single but discontinuous feature, and specifies where the location corresponding to the feature on the indicated sequence is found or how the feature is constructed. A list of location operators is provided below with their definitions. Location operators can be used for nucleotides only.

Location syntax	Location description
`join(location,location,...,location)`	The indicated locations are joined (placed end-to-end) to form one contiguous sequence.
`order(location,location,...,location)`	The elements are found in the specified order but nothing is implied about whether joining those elements is reasonable.
`complement(location)`	Indicates that the feature is located on the strand complementary to the sequence span specified by the location descriptor, when read in the 5’ to 3’ direction or in the direction that mimics the 5’ to 3’ direction.

68. The join and order location operators require that at least two comma-separated location descriptors be provided. Location descriptors involving sites between two adjacent residues, i.e. x^y, must not be used within a join or order location. Use of the join location operator implies that the residues described by the location descriptors are physically brought into contact by biological processes (for example, the exons that contribute to a coding region feature).

69. The location operator “complement” can be used in combination with either “join” or “order” within the same location. Combinations of “join” and “order” within the same location must not be used.

70. The following examples illustrate feature locations, as per paragraphs 64 to 69 above:

(a) locations for nucleotide and amino acid sequences:

Location Example	Description
467	Points to residue 467 in the sequence.
340..565	Points to a continuous range of residues bounded by and including residues 340 and 565.
<1	Points to a feature location before the first residue.
<345..500	Indicates that the exact lower boundary point of a feature is unknown. The location begins at some residue previous to 345 and continues to and includes residue 500.
<1..888	Indicates that the feature starts before the first sequenced residue and continues to and includes residue 888.
1..>888	Indicates that the feature starts at the first sequenced residue and continues beyond residue 888.
<1..>888	Indicates that the feature starts before the first sequenced residue and continues beyond residue 888.

(b) locations for nucleotide sequences only:

Location example	Description
123^124	Points to a site between residues 123 and 124.
join(12..78,134..202)	Indicates that regions 12 to 78 and 134 to 202 should be joined to form one contiguous sequence.
complement(34..126)	Starts at the nucleotide complementary to 126 and finishes at the nucleotide complementary to nucleotide 34 (the feature is on the strand complementary to the presented strand).
complement(join(2691..4571, 4918..5163))	Joins nucleotides 2691 to 4571 and 4918 to 5163, then complements the joined segments (the feature is on the strand complementary to the presented strand).
join(complement(4918..5163), complement(2691..4571))	Complements regions 4918 to 5163 and 2691 to 4571, then joins the complemented segments (the feature is on the strand complementary to the presented strand).

(c) locations for amino acid sequences only:

Location example	Description
340..565	Indicates that the amino acids at positions 340 and 565 are joined by an intrachain linkage when used with a feature that indicates an intrachain cross-link, such as “CROSSLNK” or “DISULFID”.

71. In an XML instance of a sequence listing, the characters “<” and “>” in a location descriptor must be replaced by the appropriate predefined entities (see paragraph 41). For example:

Feature location "<1":
```
<INSDFeature_location>&lt;1</INSDFeature_location>
```

Feature location "1..>888":
```
<INSDFeature_location>1..&gt;888</INSDFeature_location>
```

Feature qualifiers

72. Qualifiers are used to supply information about features in addition to that conveyed by the feature key and feature location. There are three types of value formats to accommodate different types of information conveyed by qualifiers, namely:

(a) free text (see paragraphs 85 to 87);

(b) controlled vocabulary or enumerated values (e.g., a number or date); and

(c) sequences.

73. Section 6 of Annex I provides the exclusive listing of qualifiers and their specified value formats, if any, for each nucleotide sequence feature key and Section 8 provides the exclusive listing of qualifiers and their specified value formats, if any, for each amino acid sequence feature key.

74. Any sequence encompassed by paragraph 7 which is provided as a qualifier value must be separately included in the sequence listing and assigned its own sequence identification number (see paragraph 10).

Mandatory feature qualifiers

75. One mandatory feature key, i.e., “source” for nucleotide sequences and amino acid sequences, requires two mandatory qualifiers, “organism” and “mol_type”. Some optional feature keys also require mandatory qualifiers.

Qualifier elements

76. The element `INSDFeature_quals` contains one or more `INSDQualifier` elements. Each `INSDQualifier` element represents a single qualifier and consists of three dependent elements and one optional attribute as follows:

Element/Attribute	Description	Mandatory/Optional
`INSDQualifier_name`	Name of the qualifier (see Annex I, Sections 6 and 8)	Mandatory
`INSDQualifier_value`	Value of the qualifier, if any, in the specified format (see Annex I, Sections 6 and 8) and composed in the characters as set forth in paragraph 40(b).	Mandatory, when specified (see paragraph 87 and Annex I, Sections 6 and 8)
`NonEnglishQualifier_value`	Value of the qualifier, if any, in the specified format (see Annex I, Sections 6 and 8) and composed in the characters as set forth in paragraph 40(a).	Mandatory, when specified (see paragraph 87 and Annex I, Sections 6 and 8)
`id`	A qualifier with a language-dependent free text value may be uniquely identified by using the optional XML attribute 'id' in the element INSDQualifier (see paragraph 87(d)). The value of the 'id' attribute must start with the letter 'q' and continue with any positive integer. The value of an 'id' attribute must be unique to one INSDQualifier element, i.e. the attribute value must only be used once in a sequence listing file.	Optional

77. The organism qualifier, i.e., “organism” for nucleotide sequences (see Annex I, Section 6) and “organism" for amino acid sequences (see Annex I, Section 8) must disclose the source, i.e., a single organism or origin, of the sequence. Organism designations should be selected from a taxonomy database.

78. If the sequence is naturally occurring and the source organism has a Latin genus and species designation, that designation must be used as the qualifier value. The preferred English common name may be specified using the qualifier "note" for nucleotide sequences and amino acid sequences, but must not be used in the organism qualifier value.

79. The following examples illustrate the source organism of a sequence as per paragraphs 77 and 78 above:

Example 1: Source for a nucleotide sequence

```
<INSDSeq_feature-table>
    <INSDFeature>
        <INSDFeature_key>source</INSDFeature_key>
        <INSDFeature_location>1..5164</INSDFeature_location>
        <INSDFeature_quals>
            <INSDQualifier>
                <INSDQualifier_name>organism</INSDQualifier_name>
                <INSDQualifier_value>Solanum lycopersicum</INSDQualifier_value>
            </INSDQualifier>
            <INSDQualifier>
                <INSDQualifier_name>note</INSDQualifier_name>
                <INSDQualifier_value>common name: tomato</INSDQualifier_value>
            </INSDQualifier>
            <INSDQualifier>
                <INSDQualifier_name>mol_type</INSDQualifier_name>
                <INSDQualifier_value>genomic DNA</INSDQualifier_value>
            </INSDQualifier>
        </INSDFeature_quals>
    </INSDFeature>
</INSDSeq_feature-table>
```

Example 2: Source for an amino acid sequence

```
<INSDSeq_feature-table>
    <INSDFeature>
        <INSDFeature_key>source</INSDFeature_key>
        <INSDFeature_location>1..174</INSDFeature_location>
        <INSDFeature_quals>
            <INSDQualifier>
                <INSDQualifier_name>organism</INSDQualifier_name>
                <INSDQualifier_value>Homo sapiens</INSDQualifier_value>
            </INSDQualifier>
            <INSDQualifier>
                <INSDQualifier_name>mol_type</INSDQualifier_name>
                <INSDQualifier_value>protein</INSDQualifier_value>
            </INSDQualifier>
        </INSDFeature_quals>
    </INSDFeature>
</INSDSeq_feature-table>
```

80. If the sequence is naturally occurring and the source organism has a known Latin genus, but the species is unspecified or unidentified, then the organism qualifier value must indicate the Latin genus followed by "sp." For example:

```
<INSDQualifier_name>organism</INSDQualifier_name>
<INSDQualifier_value>Bacillus sp.</INSDQualifier_value>
```

81. If the sequence is naturally occurring, but the Latin organism genus and species designation is unknown, then the organism qualifier value must be indicated as "unidentified". Any known taxonomic information should be indicated in the qualifier "note"~~ for nucleotide sequences and the qualifier "note" for amino acid sequences~~. For example:

```
<INSDQualifier_name>organism</INSDQualifier_name>
<INSDQualifier_value>unidentified</INSDQualifier_value>
<INSDQualifier_name>note</INSDQualifier_name>
<INSDQualifier_value>bacterium B8</INSDQualifier_value>
```

82. If the sequence is naturally occurring and the source organism does not have a Latin genus and species designation, such as a virus, then another acceptable scientific name (e.g., "Canine adenovirus type 2") must be used as the organism qualifier value. For example:

```
<INSDQualifier_name>organism</INSDQualifier_name>
<INSDQualifier_value>Canine adenovirus type 2</INSDQualifier_value>
```

83. If the sequence is not naturally occurring, the organism qualifier value must be indicated as “synthetic construct”. Further information with respect to the way the sequence was generated may be specified using the qualifier “note” ~~for nucleotide sequences and the qualifier “note” for amino acid sequences~~. For example:

```
<INSDSeq_feature-table>
    <INSDFeature>
        <INSDFeature_key>source</INSDFeature_key>
        <INSDFeature_location>1..40</INSDFeature_location>
        <INSDFeature_quals>
            <INSDQualifier>
                <INSDQualifier_name>organism</INSDQualifier_name>
                <INSDQualifier_value>synthetic construct</INSDQualifier_value>
            </INSDQualifier>
            <INSDQualifier>
                <INSDQualifier_name>mol_type</INSDQualifier_name>
                <INSDQualifier_value>protein</INSDQualifier_value>
            </INSDQualifier>
            <INSDQualifier>
                <INSDQualifier_name>note</INSDQualifier_name>
                <INSDQualifier_value>synthetic peptide used as assay for
antibodies</INSDQualifier_value>
            </INSDQualifier>
        </INSDFeature_quals>
    </INSDFeature>
</INSDSeq_feature-table>
```

84. The “mol_type” qualifier for nucleotide sequences (see Annex I, Section 6) and “mol_type” qualifier for amino acid sequences (see Annex I, Section 8) must disclose the type of molecule represented in the sequence. These qualifiers are distinct from the element `INSDSeq_moltype` discussed in paragraph 54:

(a) For a nucleotide sequence, the “mol_type” qualifier value must be one of the following: “genomic DNA”, “genomic RNA”, “mRNA”, “tRNA”, “rRNA”, “other RNA”, “other DNA”, “transcribed RNA”, “viral cRNA”, “unassigned DNA”, or “unassigned RNA”. If the sequence is not naturally occurring, i.e. the value of the “organism” qualifier is “synthetic construct”, the “mol_type” qualifier value must be either “other RNA” or “other DNA”;

(b) For an amino acid sequences, the “mol_type” qualifier value is “protein”.

Free text

85. Free text, as indicated in paragraph 3 (n), is a type of value format for certain qualifiers presented in the form of a descriptive text phrase or other specified format (as indicated in Annex I).

86. The use of free text must be limited to a few short terms indispensable for the understanding of a characteristic of the sequence. For each qualifier other than the "translation" qualifier, the free text must not exceed 1000 characters.

87. Language-dependent free text, as indicated in paragraph 3 (o), is the free text value of certain qualifiers that is language-dependent in that it may require translation for international, national or regional procedures. Qualifiers for nucleotide sequences with a language-dependent free text value format are identified in Annex I, Section 6, Table 5. Qualifiers for amino acid sequences with a language-dependent free text value format are identified in Annex I, Section 8, Table 6.

(a) Language-dependent free text must be presented in the `INSDQualifier_value` element in English, or in the `NonEnglishQualifier_value` element in a language other than English, or in both elements. Note that if an organism name is a Latin genus and species name, no translation is required. Technical terms and proper names originating from non-English words that are used internationally are considered English for the purpose of the value of the `INSDQualifier_value` element (e.g., ‘in vitro’, ‘in vivo’).

(b) If a `NonEnglishQualifier_value` element is present in a sequence listing, the appropriate language code (see reference in paragraph 9 to ISO 639-1:2002) must be indicated in the `nonEnglishFreeTextLanguageCode` attribute in the root element (see paragraph 43). All `NonEnglishQualifier_value` elements in a single sequence listing must have values in the language indicated in the `nonEnglishFreeTextLanguageCode` attribute. The `NonEnglishQualifier_value` element is permitted only for qualifiers that have a language-dependent free text value format.

(c) Where NonEnglishQualifier_value and INSDQualifier_value are both present for a single qualifier, the information contained in the two elements must be equivalent. One of the following conditions must be true: NonEnglishQualifier_value contains a translation of the value of INSDQualifier_value; or, INSDQualifier_value contains a translation of the value of NonEnglishQualifier_value; or, both elements contain a translation of the qualifier value from the language specified in the originalFreeTextLanguageCode attribute (see paragraph 43).

(d) For qualifiers with a language-dependent free text value, the INSDQualifier element may include an optional attribute id. The value of this attribute must be in the format "q" followed by a positive integer, e.g. "q23", and must be unique to one INSDQualifier element, i.e. the attribute value must only be used once in a sequence listing file.

88. The following examples illustrate the presentation of language-dependent free text as discussed in paragraph 87.

Example 1: language-dependent free text in an INSDQualifier_value element:

```
<INSDFeature>
      <INSDFeature_key>regulatory</INSDFeature_key>
      <INSDFeature_location>1..60</INSDFeature_location>
      <INSDFeature_quals>
        <INSDQualifier id="q1">
               <INSDQualifier_name>function</INSDQualifier_name>
               <INSDQualifier_value>binds to regulatory protein Est3</INSDQualifier_value>
        </INSDQualifier>
      </INSDFeature_quals>
</INSDFeature>
```

Example 2: language-dependent free text in an INSDQualifier_value element and a NonEnglishQualifier_value element:

```
<INSDFeature>
        <INSDFeature_key>ACT_SITE</INSDFeature_key>
        <INSDFeature_location>51..64</INSDFeature_location>
        <INSDFeature_quals>
            <INSDQualifier id="q45">
                <INSDQualifier_name>note</INSDQualifier_name>
                <INSDQualifier_value>cleaves carbohydrate chain</INSDQualifier_value>
                <NonEnglishQualifier_value>clive la chaîne glucidique
                </NonEnglishQualifier_value>
            </INSDQualifier>
        </INSDFeature_quals>
</INSDFeature>
```

Example 3: language-dependent free text in a NonEnglishQualifier_value element:

```
<INSDFeature>
        <INSDFeature_key>ACT_SITE</INSDFeature_key>
        <INSDFeature_location>51..64</INSDFeature_location>
        <INSDFeature_quals>
            <INSDQualifier id="q1034">
                <INSDQualifier_name>note</INSDQualifier_name>
                <NonEnglishQualifier_value>clive la chaîne glucidique
                </NonEnglishQualifier_value>
            </INSDQualifier>
        </INSDFeature_quals>
</INSDFeature>
```

Coding sequences

89. The “CDS” feature key may be used to identify coding sequences, i.e., sequences of nucleotides which correspond to the sequence of amino acids in a protein and the stop codon. The location of the “CDS” feature in the mandatory element INSDFeature_location must include the stop codon.

90. The “transl_table” and “translation” qualifiers may be used with the “CDS” feature key (see Annex I). Where the “transl_table” qualifier is not used, the use of the Standard Code Table (see Annex I, Section 9, Table 7) is assumed.

91. The “transl_except” qualifier must be used with the “CDS” feature key and the “translation” qualifier to identify a codon that encodes either pyrrolysine or selenocysteine.

92. An amino acid sequence encoded by ~~the~~ a coding sequence and disclosed in a “translation” qualifier that is encompassed by paragraph 7 must be included in the sequence listing and assigned its own sequence identification number. The sequence identification number assigned to the amino acid sequence must be provided as the value in the qualifier “protein_id” with the “CDS” feature key. The “organism” qualifier of the “source” feature key for the amino acid sequence must be identical to that of its coding sequence. For example:

```
<INSDFeature>
    <INSDFeature_key>CDS</INSDFeature_key>
    <INSDFeature_location>1..507</INSDFeature_location>
    <INSDFeature_quals>
        <INSDQualifier>
            <INSDQualifier_name>transl_table</INSDQualifier_name>
            <INSDQualifier_value>11</INSDQualifier_value>
        </INSDQualifier>
        <INSDQualifier>
            <INSDQualifier_name>translation</INSDQualifier_name>
            <INSDQualifier_value>MLVHLERTTIMFDFSSLINLPLIWGLLIAIAVLLYILMDGFDLGIGILL
            PFAPSDKCRDHMISSIAPFWDGNETWLVLGGGGLFAAFPLAYSILMPAFYIPIIIMLLGLIVRGVSFEFR
            FKAEGKYRRLWDYAFHFGSLGAAFCQGMILGAFIHGVEVNGRNFSGGQLM
            </INSDQualifier_value>
        </INSDQualifier>
        <INSDQualifier>
        <INSDQualifier_name>protein_id</INSDQualifier_name>
        <INSDQualifier_value>89</INSDQualifier_value>
        </INSDQualifier>
    </INSDFeature_quals>
</INSDFeature>
```

Variants

93. A primary sequence and any variant of that sequence, each disclosed by enumeration of their residues and encompassed by paragraph 7, must each be included in the sequence listing and assigned their own sequence identification number.

94. Any variant sequence, disclosed as a single sequence with enumerated alternative residues at one or more positions, must be included in the sequence listing and should be represented by a single sequence, wherein the enumerated alternative residues are represented by the most restrictive ambiguity symbol (see paragraphs 15 and 27).

95. Any variant sequence, disclosed only by reference to deletion(s), insertion(s), or substitution(s) in a primary sequence ~~in the sequence listing~~, should be included in the sequence listing. Where included in the sequence listing, such a variant sequence:

(a) may be represented by annotation of the primary sequence, where it contains variation(s) at a single location or multiple distinct locations and the occurrence of those variations are independent;

(b) should be represented as a separate sequence and assigned its own sequence identification number, where it contains variations at multiple distinct locations and the occurrence of those variations are interdependent; and

(c) must be represented as a separate sequence and assigned its own sequence identification number, where it contains an inserted or substituted sequence that contains in excess of 1000 residues (see paragraph 86).

96. The table below indicates the proper use of feature keys and qualifiers for nucleic acid and amino acid sequence variants:

Type of sequence	Feature Key	Qualifier	Use
Nucleic acid	variation	replace or note	Naturally occurring mutations and polymorphisms, e.g., alleles, RFLPs.
Nucleic acid	misc_difference	replace or note	Variability introduced artificially, e.g., by genetic manipulation or by chemical synthesis.
Amino acid	VAR_SEQ	note	Variant produced by alternative splicing, alternative promoter usage, alternative initiation and ribosomal frameshifting.

Type of sequence	Feature Key	Qualifier	Use
Amino acid	VARIANT	note	Any type of variant for which VAR_SEQ is not applicable.

97. Annotation of a sequence for a specific variant must include a feature key and qualifier, as indicated in the table above, and the feature location. The value for the "replace" qualifier must be only a single alternative nucleotide or nucleotide sequence using only the symbols in set forth Section 1, Table 1, or empty. A listing of alternative residues may be provided as the value in the "note" qualifier. In particular, a listing of alternative amino acids must be provided as the value in the "note" qualifier where "X" is used in a sequence, and represents a value other than "any one of the unmodified L-alpha-amino acids 'A', 'R', 'N', 'D', 'C', 'Q', 'E', 'G', 'H', 'I', 'L', 'K', 'M', 'F', 'P', 'O', 'S', 'U', 'T', 'W', 'Y', or 'V'" (see paragraph 27). A deletion must be represented by an empty qualifier value for the "replace" qualifier or by an indication in the "note" qualifier that the residue may be deleted. An inserted or substituted residue(s) must be provided in the "replace" or "note" qualifier. The value format for the "replace" and "note" qualifiers is free text and must not exceed 1000 characters, as provided in paragraph 86. See paragraph 100 for sequences encompassed by paragraph 7 that are provided as an insertion or a substitution in a qualifier value.

98. The symbols set forth in Annex I (see Sections 1 to 4, Tables 1 to 4, respectively) should be used to represent variant residues where appropriate. For the "note" qualifier, where the variant residue is a modified residue not set forth in Tables 2 or 4 of Annex I, the complete unabbreviated name of the modified residue must be provided as the qualifier value. Modified residues must be further described in the feature table as provided in paragraph 17 or 30.

99. The following examples illustrate the representation of variants as per paragraphs 95 to 98 above:

Example 1: Feature key "misc_difference" for enumerated alternative nucleotides.
The "n" at position 53 of the sequence can be one of five alternative nucleotides.

```
<INSDFeature>
    <INSDFeature_key>misc_difference</INSDFeature_key>
    <INSDFeature_location>53</INSDFeature_location>
    <INSDFeature_quals>
        <INSDQualifier>
            <INSDQualifier_name>note</INSDQualifier_name>
            <INSDQualifier_value>w, cmnm5s2u, mam5u, mcm5s2u, or
p</INSDQualifier_value>
        </INSDQualifier>
    </INSDFeature_quals>
</INSDFeature>
<INSDFeature>
    <INSDFeature_key>modified_base</INSDFeature_key>
    <INSDFeature_location>53</INSDFeature_location>
    <INSDFeature_quals>
        <INSDQualifier>
            <INSDQualifier_name>mod_base</INSDQualifier_name>
            <INSDQualifier_value>OTHER</INSDQualifier_value>
         </INSDQualifier>
         <INSDQualifier>
            <INSDQualifier_name>note</INSDQualifier_name>
            <INSDQualifier_value>cmnm5s2u, mam5u, mcm5s2u, or p</INSDQualifier_value>
        </INSDQualifier>
    </INSDFeature_quals>
</INSDFeature>
```

Example 2: Feature key "misc_difference" for a deletion in a nucleotide sequence.
The nucleotide at position 413 of the sequence is deleted.

```
<INSDFeature>
    <INSDFeature_key>misc_difference</INSDFeature_key>
    <INSDFeature_location>413</INSDFeature_location>
    <INSDFeature_quals>
        <INSDQualifier>
            <INSDQualifier_name>replace</INSDQualifier_name>
            <INSDQualifier_value></INSDQualifier_value>
        </INSDQualifier>
    </INSDFeature_quals>
</INSDFeature>
```

Example 3: Feature key “misc_difference” for an insertion in a nucleotide sequence.
The sequence “atgccaaatat” is inserted between positions 100 and 101 of the primary sequence.

```
<INSDFeature>
    <INSDFeature_key>misc_difference</INSDFeature_key>
    <INSDFeature_location>100^101</INSDFeature_location>
    <INSDFeature_quals>
        <INSDQualifier>
            <INSDQualifier_name>replace</INSDQualifier_name>
            <INSDQualifier_value>atgccaaatat</INSDQualifier_value>
        </INSDQualifier>
    </INSDFeature_quals>
</INSDFeature>
```

Example 4: Feature key “variation” for a substitution in a nucleotide sequence.
A cytosine replaces the nucleotide given in position 413 of the sequence.

```
<INSDFeature>
    <INSDFeature_key>variation</INSDFeature_key>
    <INSDFeature_location>413</INSDFeature_location>
    <INSDFeature_quals>
        <INSDQualifier>
            <INSDQualifier_name>replace</INSDQualifier_name>
            <INSDQualifier_value>c</INSDQualifier_value>
        </INSDQualifier>
    </INSDFeature_quals>
</INSDFeature>
```

Example 5: Feature key “VARIANT” for a substitution in an amino acid sequence.
The amino acid given in position 100 of the sequence can be replaced by `I`, `A`, `F`, `Y`, `aIle`, `MeIle`, or `Nle`.

```
<INSDFeature>
    <INSDFeature_key>VARIANT</INSDFeature_key>
    <INSDFeature_location>100</INSDFeature_location>
    <INSDFeature_quals>
        <INSDQualifier>
            <INSDQualifier_name>note</INSDQualifier_name>
            <INSDQualifier_value>I, A, F, Y, aIle, MeIle, or Nle
          </INSDQualifier_value>
        </INSDQualifier>
    </INSDFeature_quals>
</INSDFeature>
<INSDFeature>
    <INSDFeature_key>MOD_RES</INSDFeature_key>
    <INSDFeature_location>100</INSDFeature_location>
    <INSDFeature_quals>
        <INSDQualifier>
            <INSDQualifier_name>note</INSDQualifier_name>
            <INSDQualifier_value>aIle, MeIle, or Nle</INSDQualifier_value>
        </INSDQualifier>
    </INSDFeature_quals>
</INSDFeature>
```

Example 6: Feature key “VARIANT” for a substitution in an amino acid sequence.
The amino acid given in position 100 of the sequence can be replaced by any amino acid except for Lys, Arg or His.

```
<INSDFeature>
    <INSDFeature_key>VARIANT</INSDFeature_key>
    <INSDFeature_location>100</INSDFeature_location>
    <INSDFeature_quals>
        <INSDQualifier>
            <INSDQualifier_name>note</INSDQualifier_name>
            <INSDQualifier_value>not K, R, or H</INSDQualifier_value>
        </INSDQualifier>
    </INSDFeature_quals>
</INSDFeature>
```

100. A sequence encompassed by paragraph 7 that is provided as an insertion or a substitution in a qualifier value for a primary sequence annotation must also be included in the sequence listing and assigned its own sequence identification number.

[Annex I follows]

ANNEX I

CONTROLLED VOCABULARY

Version ~~1.7~~ 2.0

*Revision approved by the Committee on WIPO Standards (CWS)
at its ~~eleventh~~ thirteenth session on ~~December 8, 2023~~ November 14, 2025*

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SECTION 1: LIST OF NUCLEOTIDES

The nucleotide base symbols to be used in sequence listings are presented in Table 1. The symbol "t" will be construed as thymine in DNA and uracil in RNA when it is used with no further description. Where an ambiguity symbol (representing two or more bases in the alternative) is appropriate, the most restrictive symbol should be used. For example, if a base in a given position could be "a or g," then "r" should be used, rather than "n". The symbol "n" will be construed as "a or c or g or t/u" when it is used with no further description.

Table 1: List of nucleotides symbols

Symbol	Definition
a	adenine
c	cytosine
g	guanine
t	thymine in DNA/uracil in RNA (t/u)
m	a or c
r	a or g
w	a or t/u
s	c or g
y	c or t/u
k	g or t/u
v	a or c or g; not t/u
h	a or c or t/u; not g
d	a or g or t/u; not c
b	c or g or t/u; not a
n	a or c or g or t/u; "unknown" or "other"

SECTION 2: LIST OF MODIFIED NUCLEOTIDES

The abbreviations listed in Table 2 are the only permitted values for the mod_base qualifier. Where a specific modified nucleotide is not present in the table below, then the abbreviation "OTHER" must be used as its value. If the abbreviation is "OTHER", then the complete unabbreviated name of the modified ~~base~~ nucleotide must be provided in a note qualifier. The abbreviations provided in Table 2 must not be used in the sequence itself.

Table 2: List of modified nucleotides

Abbreviation	Definition
ac4c	4-acetylcytidine
chm5u	5-(carboxyhydroxylmethyl)uridine
cm	2'-O-methylcytidine
cmnm5s2u	5-carboxymethylaminomethyl-2-thiouridine
cmnm5u	5-carboxymethylaminomethyluridine
dhu	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

Abbreviation	Definition
m4c	N4-methylcytosine
m5c	5-methylcytidine
m6a	N6-methyladenosine
m7g	7-methylguanosine
mam5u	5-methylaminomethyluridine
mam5s2u	5-methylaminomethyl-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-methyl-carbamoyl)threonine
mv	uridine-5-oxoacetic acid-methylester
o5u	uridine-5-oxyacetic acid (v)
osyw	wybutoxosine
p	pseudouridine
q	queuosine
s2c	2-thiocytidine
s2t	5-methyl-2-thiouridine
s2u	2-thiouridine
s4u	4-thiouridine
m5u	5-methyluridine
t6a	N-((9-beta-D-ribofuranosylpurine-6-yl)carbamoyl)threonine
tm	2'-O-methyl-5-methyluridine
um	2'-O-methyluridine
yw	wybutosine
x	3-(3-amino-3-carboxypropyl)uridine, (acp3)u
OTHER	(requires note qualifier)

SECTION 3: LIST OF AMINO ACIDS

The amino acid symbols to be used in sequence are presented in Table 3. Where an ambiguity symbol (representing two or more amino acids in the alternative) is appropriate, the most restrictive symbol should be used. For example, if an amino acid in a given position could be aspartic acid or asparagine, the symbol "B" should be used, rather than "X". The symbol "X" will be construed as any one of the unmodified L-alpha-amino acids "A", "R", "N", "D", "C", "Q", "E", "G", "H", "I", "L", "K", "M", "F", "P", "O", "S", "U", "T", "W", "Y", or "V", when it is used with no further description.

Table 3: List of amino acids symbols

Symbol	Definition
A	Alanine
R	Arginine
N	Asparagine
D	Aspartic acid (Aspartate)
C	Cysteine
Q	Glutamine
E	Glutamic acid (Glutamate)
G	Glycine
H	Histidine
I	Isoleucine
L	Leucine
K	Lysine
M	Methionine
F	Phenylalanine
P	Proline
O	Pyrrolysine
S	Serine
U	Selenocysteine
T	Threonine
W	Tryptophan
Y	Tyrosine
V	Valine
B	Aspartic acid or Asparagine
Z	Glutamine or Glutamic acid
J	Leucine or Isoleucine
X	A or R or N or D or C or Q or E or G or H or I or L or K or M or F or P or O or S or U or T or W or Y or V; "unknown" or "other"

SECTION 4: LIST OF MODIFIED AMINO ACIDS

Table 4 lists the only permitted abbreviations for a modified amino acid in the mandatory qualifier "note" for feature keys "MOD_RES" or "SITE". The value for the qualifier "note" must be either an abbreviation from this table, where appropriate, or the complete, unabbreviated name of the modified amino acid. The abbreviations (or full names) provided in this table must not be used in the sequence itself.

Table 4: List of modified amino acids

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

SECTION 5: FEATURE KEYS FOR NUCLEOTIDE SEQUENCES

This section contains the list of allowed feature keys to be used for nucleotide sequences, and lists mandatory and optional qualifiers. The feature keys are listed in alphabetic order. The feature keys can be used for either DNA or RNA unless otherwise indicated under "Molecule scope". Certain Feature Keys may be appropriate for use with artificial sequences in addition to the specified "organism scope".

Feature key names must be used in the XML instance of the sequence listing exactly as they appear following "Feature key" in the descriptions below, except for the feature keys 3'UTR and 5'UTR. See "Comment" in the description for the 3'UTR and 5'UTR feature keys.

5.1.	Feature Key	C_region
	Definition	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
	Optional qualifiers	allele gene gene_synonym map note product pseudo pseudogene standard_name
	Organism scope	eukaryotes

5.2.	Feature Key	CDS
	Definition	coding sequence; sequence of nucleotides that corresponds with the sequence of amino acids in a protein (location includes stop codon); feature may include amino acid conceptual translation
	Optional qualifiers	allele circular_RNA codon_start EC_number exception function gene gene_synonym map note number operon product protein_id pseudo pseudogene ribosomal_slippage standard_name translation transl_except transl_table trans_splicing

	Comment	codon_start qualifier has valid value of 1 or 2 or 3, indicating the offset at which the first complete codon of a coding feature can be found, relative to the first base of that feature; transl_table defines the genetic code table used if other than the Standard or universal genetic code table; genetic code exceptions outside the range of the specified tables are reported in transl_except qualifier; only one of the qualifiers translation, pseugogene or pseudo are permitted with a CDS feature key; when the translation qualifier is used, the protein_id qualifier is mandatory if the translation product contains four or more specifically defined amino acids

5.3.	Feature Key	centromere
	Definition	region of biological interest identified as a centromere and which has been experimentally characterized
	Optional qualifiers	note standard_name
	Comment	the centromere feature describes the interval of DNA that corresponds to a region where chromatids are held and a kinetochore is formed

5.4.	Feature Key	D-loop
	Definition	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
	Optional qualifiers	allele gene gene_synonym map note
	Molecule scope	DNA

5.5.	Feature Key	D_segment
	Definition	Diversity segment of immunoglobulin heavy chain, and T-cell receptor beta chain
	Optional qualifiers	allele gene gene_synonym map note product pseudo pseudogene standard_name
	Organism scope	eukaryotes

5.6.	Feature Key	exon
	Definition	region of genome that codes for portion of spliced mRNA,rRNA and tRNA; may contain 5'UTR, all CDSs and 3' UTR
	Optional qualifiers	allele EC_number function gene gene_synonym map note number product pseudo pseudogene standard_name trans_splicing

5.7.	Feature Key	gene
	Definition	region of biological interest identified as a gene and for which a name has been assigned
	Optional qualifiers	allele function gene gene_synonym map note operon product pseudo pseudogene phenotype standard_name trans_splicing
	Comment	the gene feature describes the interval of DNA that corresponds to a genetic trait or phenotype; the feature is, by definition, not strictly bound to its positions at the ends; it is meant to represent a region where the gene is located.

5.8.	Feature Key	iDNA
	Definition	intervening DNA; DNA which is eliminated through any of several kinds of recombination
	Optional qualifiers	allele function gene gene_synonym map note number standard_name
	Molecule scope	DNA
	Comment	e.g., in the somatic processing of immunoglobulin genes.

5.9.	Feature Key	intron
	Definition	a segment of DNA that is transcribed, but removed from within the transcript by splicing together the sequences (exons) on either side of it
	Optional qualifiers	allele function gene gene_synonym map note number pseudo pseudogene standard_name trans_splicing

5.10.	Feature Key	J_segment
	Definition	joining segment of immunoglobulin light and heavy chains, and T-cell receptor alpha, beta, and gamma chains
	Optional qualifiers	allele gene gene_synonym map note product pseudo pseudogene standard_name
	Organism scope	eukaryotes

5.11.	Feature Key	mat_peptide
	Definition	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)
	Optional qualifiers	allele EC_number function gene gene_synonym map note product pseudo pseudogene standard_name

5.12.	Feature Key	misc_binding
	Definition	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)
	Mandatory qualifiers	bound_moiety
	Optional qualifiers	allele function gene gene_synonym map note
	Comment	note that the regulatory feature key and regulatory_class qualifier with the value “ribosome_binding_site” must be used for describing ribosome binding sites

5.13.	Feature Key	misc_difference
	Definition	featured sequence differs from the presented sequence at this location and cannot be described by any other Difference key (variation, or modified_base)
	Optional qualifiers	allele clone compare gene gene_synonym map note phenotype replace standard_name
	Comment	the misc_difference feature key must be used to describe variability introduced artificially, e.g., by genetic manipulation or by chemical synthesis; use the replace qualifier to annotate a deletion, insertion, or substitution. The variation feature key must be used to describe naturally occurring genetic variability.

5.14.	Feature Key	misc_feature
	Definition	region of biological interest which cannot be described by any other feature key; a new or rare feature
	Optional qualifiers	allele function gene gene_synonym map note number phenotype product pseudo pseudogene standard_name
	Comment	this key should not be used when the need is merely to mark a region in order to comment on it or to use it in another feature’s location

5.15.	Feature Key	misc_recomb
	Definition	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 or qualifiers of source key (proviral)
	Optional qualifiers	allele gene gene_synonym map note recombination_class standard_name
	Molecule scope	DNA

5.16.	Feature Key	misc_RNA
	Definition	any transcript or RNA product that cannot be defined by other RNA keys (prim_transcript, precursor_RNA, mRNA, 5'UTR, 3'UTR, exon, CDS, sig_peptide, transit_peptide, mat_peptide, intron, polyA_site, ncRNA, rRNA and tRNA)
	Optional qualifiers	allele function gene gene_synonym map note operon product pseudo pseudogene standard_name trans_splicing

5.17.	Feature Key	misc_structure
	Definition	any secondary or tertiary nucleotide structure or conformation that cannot be described by other Structure keys (stem_loop and D-loop)
	Optional qualifiers	allele function gene gene_synonym map note standard_name

5.18.	Feature Key	mobile_element
	Definition	region of genome containing mobile elements
	Mandatory qualifiers	mobile_element_type
	Optional qualifiers	allele function gene gene_synonym map note rpt_family

		rpt_type standard_name
5.19.	Feature Key	modified_base
	Definition	the indicated nucleotide is a modified nucleotide and should be substituted for by the indicated molecule (given in the mod_base qualifier value)
	Mandatory qualifiers	mod_base
	Optional qualifiers	allele frequency gene gene_synonym map note
	Comment	value for the mandatory mod_base qualifier is limited to the restricted vocabulary for modified base abbreviations in Section 2 of this Annex.
5.20.	Feature Key	mRNA
	Definition	messenger RNA; includes 5' untranslated region (5'UTR), coding sequences (CDS, exon) and 3' untranslated region (3'UTR)
	Optional qualifiers	allele circular_RNA function gene gene_synonym map note operon product pseudo pseudogene standard_name trans_splicing
5.21.	Feature Key	ncRNA
	Definition	a non-protein-coding gene, other than ribosomal RNA and transfer RNA, the functional molecule of which is the RNA transcript
	Mandatory qualifiers	ncRNA_class
	Optional qualifiers	allele function gene gene_synonym map note operon product pseudo pseudogene standard_name trans_splicing
	Comment	the ncRNA feature must not be used for ribosomal and transfer RNA annotation, for which the rRNA and tRNA feature keys must be used, respectively

5.22.	Feature Key	N_region
	Definition	extra nucleotides inserted between rearranged immunoglobulin segments
	Optional qualifiers	allele gene gene_synonym map note product pseudo pseudogene standard_name
	Organism scope	eukaryotes

5.23.	Feature Key	operon
	Definition	region containing polycistronic transcript including a cluster of genes that are under the control of the same regulatory sequences/promoter and in the same biological pathway
	Mandatory qualifiers	operon
	Optional qualifiers	allele function map note phenotype pseudo pseudogene standard_name

5.24.	Feature Key	oriT
	Definition	origin of transfer; region of a DNA molecule where transfer is initiated during the process of conjugation or mobilization
	Optional qualifiers	allele bound_moiety direction gene gene_synonym map note rpt_family rpt_type rpt_unit_range rpt_unit_seq standard_name
	Molecule Scope	DNA
	Comment	rep_origin must be used to describe origins of replication; direction qualifier has permitted values left, right, and both, however only left and right are valid when used in conjunction with the oriT feature; origins of transfer can be present in the chromosome; plasmids can contain multiple origins of transfer

5.25.	Feature Key	polyA_site
	Definition	site on an RNA transcript to which will be added adenine residues by post-transcriptional polyadenylation
	Optional qualifiers	allele gene gene_synonym map note
	Organism scope	eukaryotes and eukaryotic viruses

5.26.	Feature Key	precursor_RNA
	Definition	any RNA species that is not yet the mature RNA product; may include ncRNA, rRNA, tRNA, 5' untranslated region (5'UTR), coding sequences (CDS, exon), intervening sequences (intron) and 3' untranslated region (3'UTR)
	Optional qualifiers	allele function gene gene_synonym map note operon product standard_name trans_splicing
	Comment	used for RNA which may be the result of post-transcriptional processing; if the RNA in question is known not to have been processed, use the prim_transcript key

5.27.	Feature Key	prim_transcript
	Definition	primary (initial, unprocessed) transcript; may include ncRNA, rRNA, tRNA, 5' untranslated region (5'UTR), coding sequences (CDS, exon), intervening sequences (intron) and 3' untranslated region (3'UTR)
	Optional qualifiers	allele function gene gene_synonym map note operon standard_name

5.28.	Feature Key	primer_bind
	Definition	non-covalent primer binding site for initiation of replication, transcription, or reverse transcription; includes site(s) for synthetic e.g., PCR primer elements
	Optional qualifiers	allele gene gene_synonym map note standard_name
	Comment	used to annotate the site on a given sequence to which a primer molecule binds -

		not intended to represent the sequence of the primer molecule itself; since PCR reactions most often involve pairs of primers, a single primer_bind key may use the order(location,location) operator with two locations, or a pair of primer_bind keys may be used
5.29.	Feature Key	propeptide
	Definition	propeptide coding sequence; coding sequence for the domain of a proprotein that is cleaved to form the mature protein product.
	Optional qualifiers	allele function gene gene_synonym map note product pseudo pseudogene standard_name
5.30.	Feature Key	protein_bind
	Definition	non-covalent protein binding site on nucleic acid
	Mandatory qualifiers	bound_moiety
	Optional qualifiers	allele function gene gene_synonym map note operon standard_name
	Comment	note that the regulatory feature key and regulatory_class qualifier with the value “ribosome_binding_site” must be used to describe ribosome binding sites
5.31.	Feature Key	regulatory
	Definition	any region of a sequence that functions in the regulation of transcription, translation, replication or chromatin structure;
	Mandatory qualifiers	regulatory_class
	Optional qualifiers	allele bound_moiety function gene gene_synonym map note operon phenotype pseudo pseudogene standard_name

5.32.	Feature Key	repeat_region
	Definition	region of genome containing repeating units
	Optional qualifiers	allele function gene gene_synonym map note rpt_family rpt_type rpt_unit_range rpt_unit_seq satellite standard_name

5.33.	Feature Key	rep_origin
	Definition	origin of replication; starting site for duplication of nucleic acid to give two identical copies
	Optional Qualifiers	allele direction function gene gene_synonym map note standard_name
	Comment	direction qualifier has valid values: left, right, or both

5.34.	Feature Key	rRNA
	Definition	mature ribosomal RNA; RNA component of the ribonucleoprotein particle (ribosome) which assembles amino acids into proteins
	Optional qualifiers	allele function gene gene_synonym map note operon product pseudo pseudogene standard_name
	Comment	rRNA sizes should be annotated with the product qualifier

5.35.	Feature Key	S_region
	Definition	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
	Optional qualifiers	allele gene gene_synonym map note product pseudo pseudogene standard_name
	Organism scope	eukaryotes

5.36.	Feature Key	sig_peptide
	Definition	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
	Optional qualifiers	allele function gene gene_synonym map note product pseudo pseudogene standard_name

5.37.	Feature Key	source
	Definition	identifies the source of the sequence; this key is mandatory; every sequence will have a single source key spanning the entire sequence
	Mandatory qualifiers	organism mol_type
	Optional qualifiers	cell_line cell_type chromosome clone clone_lib collected_by collection_date cultivar dev_stage ecotype environmental_sample germline haplogroup haplotype host identified_by isolate isolation_source lab_host lat_lon macronuclear map mating_type note organelle PCR_primers plasmid pop_variant proviral rearranged segment serotype serovar sex strain sub_clone sub_species sub_strain tissue_lib tissue_type variety
	Molecule scope	any

5.38.	Feature Key	stem_loop
	Definition	hairpin; a double-helical region formed by base-pairing between adjacent (inverted) complementary sequences in a single strand of RNA or DNA
	Optional qualifiers	allele function gene gene_synonym map note operon standard_name

5.39.	Feature Key	STS
	Definition	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
	Optional qualifiers	allele gene gene_synonym map note standard_name
	Molecule scope	DNA
	Comment	STS location to include primer(s) in primer_bind key or primers

5.40.	Feature Key	telomere
	Definition	region of biological interest identified as a telomere and which has been experimentally characterized
	Optional qualifiers	note rpt_type rpt_unit_range rpt_unit_seq standard_name
	Comment	the telomere feature describes the interval of DNA that corresponds to a specific structure at the end of the linear eukaryotic chromosome which is required for the integrity and maintenance of the end; this region is unique compared to the rest of the chromosome and represents the physical end of the chromosome

5.41.	Feature Key	tmRNA
	Definition	transfer messenger RNA; tmRNA acts as a tRNA first, and then as an mRNA that encodes a peptide tag; the ribosome translates this mRNA region of tmRNA and attaches the encoded peptide tag to the C-terminus of the unfinished protein; this attached tag targets the protein for destruction or proteolysis
	Optional qualifiers	allele function gene gene_synonym map note product pseudo pseudogene standard_name tag_peptide

5.42.	Feature Key	transit_peptide
	Definition	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
	Optional qualifiers	allele function gene gene_synonym map note product pseudo pseudogene standard_name

5.43.	Feature Key	tRNA
	Definition	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
	Optional qualifiers	allele circular_RNA anticodon function gene gene_synonym map note operon product pseudo pseudogene standard_name trans_splicing

5.44.	Feature Key	unsure
	Definition	a small region of sequenced bases, generally 10 or fewer in its length, which could not be confidently identified. Such a region might contain called bases (a, t, g, or c), or a mixture of called-bases and uncalled-bases ('n').
	Optional qualifiers	allele compare gene gene_synonym map note replace
	Comment	use the replace qualifier to annotate a deletion, insertion, or substitution.

5.45.	Feature Key	V_region
	Definition	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 composed of V_segments, D_segments, N_regions, and J_segments
	Optional qualifiers	allele gene gene_synonym map note product pseudo pseudogene standard_name
	Organism scope	eukaryotes

5.46.	Feature Key	V_segment
	Definition	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
	Optional qualifiers	allele gene gene_synonym map note product pseudo pseudogene standard_name
	Organism scope	eukaryotes

5.47.	Feature Key	variation
	Definition	a related strain contains stable mutations from the same gene (e.g., RFLPs, polymorphisms, etc.) which differ from the presented sequence at this location (and possibly others)
	Optional qualifiers	allele compare frequency gene gene_synonym map note phenotype product replace standard_name
	Comment	used to describe alleles, RFLP's, and other naturally occurring mutations and polymorphisms; use the replace qualifier to annotate a deletion, insertion, or substitution; variability arising as a result of genetic manipulation (e.g., site directed mutagenesis) must be described with the misc_difference feature

5.48.	Feature Key	3'UTR
	Definition	1) region at the 3' end of a mature transcript (following the stop codon) that is not translated into a protein; 2) region at the 3' end of an RNA virus (following the last stop codon) that is not translated into a protein;
	Optional qualifiers	allele function gene gene_synonym map note standard_name trans_splicing
	Comment	The apostrophe character has special meaning in XML, and must be substituted with "'" in the value of an element. Thus "3'UTR" must be represented as "3'UTR" in the XML file, i.e., <INSDFeature_key>3'UTR</INSDFeature_key>.

5.49.	Feature Key	5'UTR
	Definition	1) region at the 5' end of a mature transcript (preceding the initiation codon) that is not translated into a protein; 2) region at the 5' end of an RNA virus (preceding the first initiation codon) that is not translated into a protein;
	Optional qualifiers	allele function gene gene_synonym map note standard_name trans_splicing
	Comment	The apostrophe character has special meaning in XML, and must be substituted with "'" in the value of an element. Thus "5'UTR" must be represented as "5'UTR" in the XML file, i.e., <INSDFeature_key>5'UTR</INSDFeature_key>.

SECTION 6: QUALIFIERS FOR NUCLEOTIDE SEQUENCES

This section contains the list of qualifiers to be used for features in nucleotide sequences. The qualifiers are listed in alphabetic order.

Where the value format is "none", the `INSDQualifier_value` element must not be used and the `NonEnglishQualifier_value` element must not be used.

Where the value format is free text that is identified as language-dependent, one of the following must be used:

1) the `INSDQualifier_value` element; or
2) the `NonEnglishQualifier_value` element; or
3) both the `INSDQualifier_value` element and the `NonEnglishQualifier_value` element.

Where the value format is something other than "none" but not identified as language-dependent free text, the `INSDQualifier_value` element must be used and the `NonEnglishQualifier_value` element must not be used.

PLEASE NOTE: Any qualifier value provided for a qualifier with a language-dependent free text value format may require translation for international, national or regional procedures. The qualifiers listed in the following table are considered to have language-dependent free text values:

Table 5: List of qualifiers with language-dependent free text values for nucleotide sequences

Section	Language-Dependent Free Text Qualifier
6.3	bound_moiety
6.5	cell_type
6.8	clone
6.9	clone_lib
6.11	collected_by
6.14	cultivar
6.15	dev_stage
6.18	ecotype
6.21	frequency
6.22	function
6.24	gene_synonym
6.26	haplogroup
6.28	host
6.29	identified_by
6.30	isolate
6.31	isolation_source
6.32	lab_host
6.36	mating_type
6.41	note
6.45	organism
6.47	phenotype
6.49	pop_variant
6.50	product
6.66	serotype
6.67	serovar
6.68	sex
6.69	standard_name
6.70	strain
6.71	sub_clone
6.72	sub_species
6.73	sub_strain
6.75	tissue_lib
6.76	tissue_type
6.81	variety

6.1.	Qualifier	allele
	Definition	name of the allele for the given gene
	Mandatory value format	free text
	Example	<INSDQualifier_value>adh1-1</INSDQualifier_value>
	Comment	all gene-related features (exon, CDS etc) for a given gene should share the same allele qualifier value; the allele qualifier value must, by definition, be different from the gene qualifier value; when used with the variation feature key, the allele qualifier value should be that of the variant.

6.2.	Qualifier	anticodon
	Definition	location of the anticodon of tRNA and the amino acid for which it codes
	Mandatory value format	(pos:<location>,aa:<amino_acid>,seq:<text>) where <location> is the position of the anticodon and <amino_acid> is the three letter abbreviation for the amino acid encoded and <text> is the sequence of the anticodon
	Example	<INSDQualifier_value>(pos:34..36,aa:Phe,seq:aaa)</INSDQualifier_value> <INSDQualifier_value>(pos:join(5,495..496),aa:Leu,seq:taa)</INSDQualifier_value> <INSDQualifier_value>(pos:complement(4156..4158),aa:Glu,seq:ttg)</INSDQualifier_value>

6.3.	Qualifier	bound_moiety
	Definition	name of the molecule/complex that may bind to the given feature
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>GAL4</INSDQualifier_value>
	Comment	A single bound_moiety qualifier is permitted on the "misc_binding", "oriT" and "protein_bind" features.

6.4.	Qualifier	cell_line
	Definition	cell line from which the sequence was obtained
	Mandatory value format	free text
	Example	<INSDQualifier_value>MCF7</INSDQualifier_value>

6.5.	Qualifier	cell_type
	Definition	cell type from which the sequence was obtained
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>leukocyte</INSDQualifier_value>

6.6.	Qualifier	chromosome
	Definition	chromosome (e.g., Chromosome number) from which the sequence was obtained
	Mandatory value format	free text
	Example	<INSDQualifier_value>1</INSDQualifier_value> <INSDQualifier_value>X</INSDQualifier_value>
6.7.	Qualifier	circular_RNA
	Definition	indicates that exons are out-of-order or overlapping because this spliced RNA product is a circular RNA (circRNA) created by backsplicing, for example when a downstream exon in the gene is located 5' of an upstream exon in the RNA product
	Value format	none
	Comment	should be used on features such as CDS, mRNA, tRNA and other features that are produced as a result of a backsplicing event. This qualifier should be used only when the splice event is indicated in the "join" operator, eg join(complement(69611..69724),139856..140087)
6.8.	Qualifier	clone
	Definition	clone from which the sequence was obtained
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>lambda-hIL7.3</INSDQualifier_value>
	Comment	a source feature must not contain more than one clone qualifier; where the sequence was obtained from multiple clones it may be further described in the feature table using the feature key misc_feature and a note qualifier to specify the multiple clones.
6.9.	Qualifier	clone_lib
	Definition	clone library from which the sequence was obtained
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>lambda-hIL7</INSDQualifier_value>
6.10.	Qualifier	codon_start
	Definition	indicates the offset at which the first complete codon of a coding feature can be found, relative to the first base of that feature.
	Mandatory value format	1 or 2 or 3
	Example	<INSDQualifier_value>2</INSDQualifier_value>

6.11.	Qualifier	collected_by
	Definition	name of persons or institute who collected the specimen
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>Dan Janzen</INSDQualifier_value>

6.12.	Qualifier	collection_date
	Definition	date that the specimen was collected.
	Mandatory value format	YYYY-MM-DD, YYYY-MM or YYYY
	Example	<INSDQualifier_value>1952-10-21</INSDQualifier_value> <INSDQualifier_value>1952-10</INSDQualifier_value> <INSDQualifier_value>1952</INSDQualifier_value>

6.13.	Qualifier	compare
	Definition	Reference details of an existing public INSD entry to which a comparison is made
	Mandatory value format	[accession-number.sequence-version]
	Example	<INSDQualifier_value>AJ634337.1</INSDQualifier_value>
	Comment	This qualifier may be used on the following features: misc_difference, unsure, and variation. Multiple compare qualifiers with different contents are allowed within a single feature. This qualifier is not intended for large-scale annotation of variations, such as SNPs.

6.14.	Qualifier	cultivar
	Definition	cultivar (cultivated variety) of plant from which sequence was obtained
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>Nipponbare</INSDQualifier_value> <INSDQualifier_value>Tenuifolius</INSDQualifier_value> <INSDQualifier_value>Candy Cane</INSDQualifier_value> <INSDQualifier_value>IR36</INSDQualifier_value>
	Comment	'cultivar' is applied solely to products of artificial selection; use the variety qualifier for natural, named plant and fungal varieties.

6.15.	Qualifier	dev_stage
	Definition	if the sequence was obtained from an organism in a specific developmental stage, it is specified with this qualifier
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>fourth instar larva</INSDQualifier_value>

6.16.	Qualifier	direction
	Definition	direction of DNA replication
	Mandatory value format	left, right, or both where left indicates toward the 5' end of the sequence (as presented) and right indicates toward the 3' end
	Example	<INSDQualifier_value>left</INSDQualifier_value>
	Comment	The values left, right, and both are permitted when the direction qualifier is used to annotate a rep_origin feature key. However, only left and right values are permitted when the direction qualifier is used to annotate an oriT feature key.

6.17.	Qualifier	EC_number
	Definition	Enzyme Commission number for enzyme product of sequence
	Mandatory value format	free text
	Example	<INSDQualifier_value>1.1.2.4</INSDQualifier_value> <INSDQualifier_value>1.1.2.-</INSDQualifier_value> <INSDQualifier_value>1.1.2.n</INSDQualifier_value> <INSDQualifier_value>1.1.2.n1</INSDQualifier_value>
	Comment	valid values for EC numbers are defined in the list prepared by the Nomenclature Committee of the International Union of Biochemistry and Molecular Biology (NC-IUBMB) (published in Enzyme Nomenclature 1992, Academic Press, San Diego, or a more recent revision thereof).The format represents a string of four numbers separated by full stops; up to three numbers starting from the end of the string may be replaced by dash "-" to indicate uncertain assignment. Symbols including an "n", e.g., "n", "n1" and so on, may be used in the last position instead of a number where the EC number is awaiting assignment. Please note that such incomplete EC numbers are not approved by NC-IUBMB.

6.18.	Qualifier	ecotype
	Definition	a population within a given species displaying genetically based, phenotypic traits that reflect adaptation to a local habitat
	Mandatory value Format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>Columbia</INSDQualifier_value>
	Comment	an example of such a population is one that has adapted hairier than normal leaves as a response to an especially sunny habitat. 'Ecotype' is often applied to standard genetic stocks of Arabidopsis thaliana, but it can be applied to any

		sessile organism.
6.19.	Qualifier	environmental_sample
	Definition	identifies sequences derived by direct molecular isolation from a bulk environmental DNA sample (by PCR with or without subsequent cloning of the product, DGGE, or other anonymous methods) with no reliable identification of the source organism. Environmental samples include clinical samples, gut contents, and other sequences from anonymous organisms that may be associated with a particular host. They do not include endosymbionts that can be reliably recovered from a particular host, organisms from a readily identifiable but uncultured field sample (e.g., many cyanobacteria), or phytoplasmas that can be reliably recovered from diseased plants (even though these cannot be grown in axenic culture)
	Value format	none
	Comment	used only with the source feature key; source feature keys containing the environmental_sample qualifier should also contain the isolation_source qualifier; a source feature including the environmental_sample qualifier must not include the strain qualifier.
6.20.	Qualifier	exception
	Definition	indicates that the coding region cannot be translated using standard biological rules
	Mandatory value format	One of the following controlled vocabulary phrases: RNA editing rearrangement required for product annotated by transcript or proteomic data
	Example	<INSDQualifier_value>RNA editing</INSDQualifier_value> <INSDQualifier_value>rearrangement required for product</INSDQualifier_value>
	Comment	only to be used to describe biological mechanisms such as RNA editing; protein translation of a CDS with an exception qualifier will be different from the corresponding conceptual translation; must not be used where transl_except qualifier would be adequate, e.g., in case of stop codon completion use.
6.21.	Qualifier	frequency
	Definition	frequency of the occurrence of a feature
	Mandatory value format	free text representing the proportion of a population carrying the feature expressed as a fraction Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>23/108</INSDQualifier_value> <INSDQualifier_value>1 in 12</INSDQualifier_value> <INSDQualifier_value>0.85</INSDQualifier_value>
6.22.	Qualifier	function
	Definition	function attributed to a sequence
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures

	Example	<INSDQualifier_value>essential for recognition of cofactor </INSDQualifier_value>
	Comment	The function qualifier is used when the gene name and/or product name do not convey the function attributable to a sequence.
6.23.	Qualifier	gene
	Definition	symbol of the gene corresponding to a sequence region
	Mandatory value format	free text
	Example	<INSDQualifier_value>ilvE</INSDQualifier_value>
	Comment	Use gene qualifier to provide the gene symbol; use standard_name qualifier to provide the full gene name.
6.24.	Qualifier	gene_synonym
	Definition	synonymous, replaced, obsolete or former gene symbol
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>Hox-3.3</INSDQualifier_value> in a feature where the gene qualifier value is Hoxc6
	Comment	used where it is helpful to indicate a gene symbol synonym; when the gene_synonym qualifier is used, a primary gene symbol must always be indicated in a gene qualifier
6.25.	Qualifier	germline
	Definition	the sequence presented has not undergone somatic rearrangement as part of an adaptive immune response; it is the unrearranged sequence that was inherited from the parental germline
	Value format	none
	Comment	germline qualifier must not be used to indicate that the source of the sequence is a gamete or germ cell; germline and rearranged qualifiers must not be used in the same source feature; germline and rearranged qualifiers must only be used for molecules that can undergo somatic rearrangements as part of an adaptive immune response; these are the T-cell receptor (TCR) and immunoglobulin loci in the jawed vertebrates, and the unrelated variable lymphocyte receptor (VLR) locus in the jawless fish (lampreys and hagfish); germline and rearranged qualifiers should not be used outside of the Craniata (taxid=89593)
6.26.	Qualifier	haplogroup
	Definition	name for a group of similar haplotypes that share some sequence variation. Haplogroups are often used to track migration of population groups.
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>H*</INSDQualifier_value>

6.27.	Qualifier	haplotype
	Definition	name for a specific set of alleles that are linked together on the same physical chromosome. In the absence of recombination, each haplotype is inherited as a unit, and may be used to track gene flow in populations.
	Mandatory value format	free text
	Example	<INSDQualifier_value>Dw3 B5 Cw1 A1</INSDQualifier_value>

6.28.	Qualifier	host
	Definition	natural (as opposed to laboratory) host to the organism from which sequenced molecule was obtained
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>Homo sapiens</INSDQualifier_value> <INSDQualifier_value>Homo sapiens 12 year old girl</INSDQualifier_value> <INSDQualifier_value>Rhizobium NGR234</INSDQualifier_value>

6.29.	Qualifier	identified_by
	Definition	name of the expert who identified the specimen taxonomically
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>John Burns</INSDQualifier_value>

6.30.	Qualifier	isolate
	Definition	individual isolate from which the sequence was obtained
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>Patient #152</INSDQualifier_value> <INSDQualifier_value>DGGE band PSBAC-13</INSDQualifier_value>

6.31.	Qualifier	isolation_source
	Definition	describes the physical, environmental and/or local geographical source of the biological sample from which the sequence was derived
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Examples	<INSDQualifier_value>rumen isolates from standard Pelleted ration-fed steer #67</INSDQualifier_value> <INSDQualifier_value>permanent Antarctic sea ice</INSDQualifier_value> <INSDQualifier_value>denitrifying activated sludge from carbon_limited continuous reactor</INSDQualifier_value>

	Comment	used only with the source feature key; source feature keys containing an environmental_sample qualifier should also contain an isolation_source qualifier
6.32.	Qualifier	lab_host
	Definition	scientific name of the laboratory host used to propagate the source organism from which the sequenced molecule was obtained
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>Gallus gallus</INSDQualifier_value> <INSDQualifier_value>Gallus gallus embryo</INSDQualifier_value> <INSDQualifier_value>Escherichia coli strain DH5 alpha</INSDQualifier_value> <INSDQualifier_value>Homo sapiens HeLa cells</INSDQualifier_value>
	Comment	the full binomial scientific name of the host organism should be used when known; extra conditional information relating to the host may also be included
6.33.	Qualifier	lat_lon
	Definition	geographical coordinates of the location where the specimen was collected
	Mandatory value format	free text - degrees latitude and longitude in format "d[d.dddd] N|S d[dd.dddd] W|E"
	Example	<INSDQualifier_value>47.94 N 28.12 W</INSDQualifier_value> <INSDQualifier_value>45.0123 S 4.1234 E</INSDQualifier_value>
6.34.	Qualifier	macronuclear
	Definition	if the sequence shown is DNA and from an organism which undergoes chromosomal differentiation between macronuclear and micronuclear stages, this qualifier is used to denote that the sequence is from macronuclear DNA
	Value format	none
6.35.	Qualifier	map
	Definition	genomic map position of feature
	Mandatory value format	free text
	Example	<INSDQualifier_value>8q12-q13</INSDQualifier_value>
6.36.	Qualifier	mating_type
	Definition	mating type of the organism from which the sequence was obtained; mating type is used for prokaryotes, and for eukaryotes that undergo meiosis without sexually dimorphic gametes
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Examples	<INSDQualifier_value>MAT-1</INSDQualifier_value> <INSDQualifier_value>plus</INSDQualifier_value>

		<INSDQualifier_value>-</INSDQualifier_value> <INSDQualifier_value>odd</INSDQualifier_value> <INSDQualifier_value>even</INSDQualifier_value>"
	Comment	mating_type qualifier values male and female are valid in the prokaryotes, but not in the eukaryotes; for more information, see the entry for the sex qualifier.
6.37.	Qualifier	mobile_element_type
	Definition	type and name or identifier of the mobile element which is described by the parent feature
	Mandatory value format	<mobile_element_type>[:<mobile_element_name>] where <mobile_element_type> is one of the following: transposon retrotransposon integron insertion sequence non-LTR retrotransposon SINE MITE LINE other
	Example	<INSDQualifier_value>transposon:Tnp9</INSDQualifier_value>
	Comment	mobile_element_type is permitted on mobile_element feature key only. Mobile element should be used to represent both elements which are currently mobile, and those which were mobile in the past. Value "other" for <mobile_element_type> requires a <mobile_element_name>
6.38.	Qualifier	mod_base
	Definition	abbreviation for a modified nucleotide ~~base~~
	Mandatory value format	modified base abbreviation chosen from this Annex, Section 2
	Example	<INSDQualifier_value>m5c</INSDQualifier_value> <INSDQualifier_value>OTHER</INSDQualifier_value>
	Comment	specific modified nucleotides not found in Section 2 of this Annex are annotated by entering OTHER as the value for the mod_base qualifier and including a note qualifier with the full name of the modified ~~base~~ nucleotide as its value
6.39.	Qualifier	mol_type
	Definition	molecule type of sequence
	Mandatory value format	One chosen from the following: genomic DNA genomic RNA mRNA tRNA rRNA other RNA other DNA transcribed RNA viral cRNA unassigned DNA unassigned RNA

	Example	<INSDQualifier_value>genomic DNA</INSDQualifier_value> <INSDQualifier_value>other RNA</INSDQualifier_value>
	Comment	mol_type qualifier is mandatory on the source feature key; the value "genomic DNA" does not imply that the molecule is nuclear (e.g., organelle and plasmid DNA must be described using "genomic DNA"); ribosomal RNA genes must be described using "genomic DNA"; "rRNA" must only be used if the ribosomal RNA molecule itself has been sequenced; values "other RNA" and "other DNA" must be applied to synthetic molecules, values "unassigned DNA", "unassigned RNA" must be applied where in vivo molecule is unknown.
6.40.	Qualifier	ncRNA_class
	Definition	a structured description of the classification of the non-coding RNA described by the ncRNA parent key
	Mandatory value format	TYPE where TYPE is one of the following controlled vocabulary terms or phrases: antisense_RNA autocatalytically_spliced_intron circRNA ribozyme hammerhead_ribozyme lncRNA RNase_P_RNA RNase_MRP_RNA telomerase_RNA guide_RNA sgRNA rasiRNA scRNA scaRNA siRNA pre_miRNA miRNA piRNA snoRNA snRNA SRP_RNA vault_RNA Y_RNA other
	Example	<INSDQualifier_value>autocatalytically_spliced_intron </INSDQualifier_value> <INSDQualifier_value>siRNA</INSDQualifier_value> <INSDQualifier_value>scRNA</INSDQualifier_value> <INSDQualifier_value>other</INSDQualifier_value>
	Comment	specific ncRNA types not yet in the ncRNA_class controlled vocabulary must be annotated by entering "other" as the ncRNA_class qualifier value, and providing a brief explanation of novel ncRNA_class in a note qualifier
6.41.	Qualifier	note
	Definition	any comment or additional information
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>A comment about the feature</INSDQualifier_value>

6.42.	Qualifier	number
	Definition	a number to indicate the order of genetic elements (e.g., exons or introns) in the 5' to 3' direction
	Mandatory value format	free text (with no whitespace characters)
	Example	<INSDQualifier_value>4</INSDQualifier_value> <INSDQualifier_value>6B</INSDQualifier_value>
	Comment	text limited to integers, letters or combination of integers and/or letters represented as a data value that contains no whitespace characters; any additional terms should be included in a standard_name qualifier. Example: a number qualifier with a value of 2A and a standard_name qualifier with a value of "long"

6.43.	Qualifier	operon
	Definition	name of the group of contiguous genes transcribed into a single transcript to which that feature belongs
	Mandatory value format	free text
	Example	<INSDQualifier_value>lac</INSDQualifier_value>

6.44.	Qualifier	organelle
	Definition	type of membrane-bound intracellular structure from which the sequence was obtained
	Mandatory value format	One of the following controlled vocabulary terms and phrases: chromatophore hydrogenosome mitochondrion nucleomorph plastid mitochondrion:kinetoplast plastid:chloroplast plastid:apicoplast plastid:chromoplast plastid:cyanelle plastid:leucoplast plastid:proplastid
	Examples	<INSDQualifier_value>chromatophore</INSDQualifier_value> <INSDQualifier_value>hydrogenosome</INSDQualifier_value> <INSDQualifier_value>mitochondrion</INSDQualifier_value> <INSDQualifier_value>nucleomorph</INSDQualifier_value> <INSDQualifier_value>plastid</INSDQualifier_value> <INSDQualifier_value>mitochondrion:kinetoplast</INSDQualifier_value> <INSDQualifier_value>plastid:chloroplast</INSDQualifier_value> <INSDQualifier_value>plastid:apicoplast</INSDQualifier_value> <INSDQualifier_value>plastid:chromoplast</INSDQualifier_value> <INSDQualifier_value>plastid:cyanelle</INSDQualifier_value> <INSDQualifier_value>plastid:leucoplast</INSDQualifier_value> <INSDQualifier_value>plastid:proplastid</INSDQualifier_value>

6.45.	Qualifier	organism
	Definition	scientific name of the organism that provided the sequenced genetic material, if known, or the available taxonomic information if the organism is unclassified; or an indication that the sequence is a synthetic construct

	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>Homo sapiens</INSDQualifier_value>
6.46.	Qualifier	PCR_primers
	Definition	PCR primers that were used to amplify the sequence. A single PCR_primers qualifier should contain all the primers used for a single PCR reaction. If multiple forward or reverse primers are present in a single PCR reaction, multiple sets of fwd_name/fwd_seq or rev_name/rev_seq values will be present
	Mandatory value format	[fwd_name: XXX1,]fwd_seq: xxxxx1,[fwd_name: XXX2,]fwd_seq: xxxxx2, [rev_name: YYY1,]rev_seq: yyyyy1,[rev_name: YYY2,]rev_seq: yyyyy2
	Example	<INSDQualifier_value>fwd_name: CO1P1, fwd_seq: ttgatttttggtcayccwgaagt,rev_name: CO1R4, rev_seq: ccwvytardcctarraartgttg</INSDQualifier_value> <INSDQualifier_value>fwd_name: hoge1, fwd_seq: cgkgtgtatcttact, rev_name: hoge2, rev_seq: cg<i>gtgtatcttact</INSDQualifier_value> <INSDQualifier_value>fwd_name: CO1P1, fwd_seq: ttgatttttggtcayccwgaagt, fwd_name: CO1P2, fwd_seq: gatacacaggtcayccwgaagt, rev_name: CO1R4, rev_seq: ccwvytardcctarraartgttg</INSDQualifier_value>
	Comment	fwd_seq and rev_seq are both mandatory; fwd_name and rev_name are both optional. Both sequences must be presented in 5' to 3' order. The sequences must be given in the symbols from Section 1 of this Annex, except for the modified bases, which must be enclosed within angle brackets < >. In XML, the angle brackets < and > must be substituted with < and > since they are reserved characters in XML.
6.47.	Qualifier	phenotype
	Definition	phenotype conferred by the feature, where phenotype is defined as a physical, biochemical or behavioural characteristic or set of characteristics
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>erythromycin resistance</INSDQualifier_value>
6.48.	Qualifier	plasmid
	Definition	name of naturally occurring plasmid from which the sequence was obtained, where plasmid is defined as an independently replicating genetic unit that cannot be described by chromosome or segment qualifiers
	Mandatory value format	free text
	Example	<INSDQualifier_value>pC589</INSDQualifier_value>
6.49.	Qualifier	pop_variant
	Definition	name of subpopulation or phenotype of the sample from which the sequence was derived
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures

	Example	<INSDQualifier_value>pop1</INSDQualifier_value> <INSDQualifier_value>Bear Paw</INSDQualifier_value>
6.50.	Qualifier	product
	Definition	name of the product associated with the feature, e.g., the mRNA of an mRNA feature, the polypeptide of a CDS, the mature peptide of a mat_peptide, etc.
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>trypsinogen</INSDQualifier_value> (when qualifier appears in CDS feature) <INSDQualifier_value>trypsin</INSDQualifier_value> (when qualifier appears in mat_peptide feature) <INSDQualifier_value>XYZ neural-specific transcript</INSDQualifier_value> (when qualifier appears in mRNA feature)
6.51.	Qualifier	protein_id
	Definition	protein sequence identification number, an integer used in a sequence listing to designate the protein sequence encoded by the coding sequence identified in the corresponding CDS feature key and translation qualifier
	Mandatory value format	an integer greater than zero
	Example	<INSDQualifier_value>89</INSDQualifier_value>
6.52.	Qualifier	proviral
	Definition	this qualifier is used to flag sequence obtained from a virus or phage that is integrated into the genome of another organism
	Value format	none
6.53.	Qualifier	pseudo
	Definition	indicates that this feature is a non-functional version of the element named by the feature key
	Value format	none
	Comment	The qualifier pseudo should be used to describe non-functional genes that are not formally described as pseudogenes, e.g., CDS has no translation due to other reasons than pseudogenization events. Other reasons may include sequencing or assembly errors. In order to annotate pseudogenes the qualifier pseudogene must be used, indicating the TYPE of pseudogene.
6.54.	Qualifier	pseudogene
	Definition	indicates that this feature is a pseudogene of the element named by the feature key
	Mandatory value format	TYPE where TYPE is one of the following controlled vocabulary terms or phrases: processed unprocessed unitary

		allelic unknown
	Example	<INSDQualifier_value>processed</INSDQualifier_value> <INSDQualifier_value>unprocessed</INSDQualifier_value> <INSDQualifier_value>unitary</INSDQualifier_value> <INSDQualifier_value>allelic</INSDQualifier_value> <INSDQualifier_value>unknown</INSDQualifier_value>
	Comment	Definitions of TYPE values: processed - the pseudogene has arisen by reverse transcription of a mRNA into cDNA, followed by reintegration into the genome. Therefore, it has lost any intron/exon structure, and it might have a pseudo-polyA-tail. unprocessed - the pseudogene has arisen from a copy of the parent gene by duplication followed by accumulation of random mutations. The changes, compared to their functional homolog, include insertions, deletions, premature stop codons, frameshifts and a higher proportion of non-synonymous versus synonymous substitutions. unitary - the pseudogene has no parent. It is the original gene, which is functional is some species but disrupted in some way (indels, mutation, recombination) in another species or strain. allelic - a (unitary) pseudogene that is stable in the population but importantly it has a functional alternative allele also in the population. i.e., one strain may have the gene, another strain may have the pseudogene. MHC haplotypes have allelic pseudogenes. unknown - the submitter does not know the method of pseudogenization.
6.55.	Qualifier	rearranged
	Definition	the sequence presented in the entry has undergone somatic rearrangement as part of an adaptive immune response; it is not the unrearranged sequence that was inherited from the parental germline
	Value format	none
	Comment	The rearranged qualifier must not be used to annotate chromosome rearrangements that are not involved in an adaptive immune response; germline and rearranged qualifiers must not be used in the same source feature; germline and rearranged qualifiers must only be used for molecules that can undergo somatic rearrangements as part of an adaptive immune response; these are the T-cell receptor (TCR) and immunoglobulin loci in the jawed vertebrates, and the unrelated variable lymphocyte receptor (VLR) locus in the jawless fish (lampreys and hagfish); germline and rearranged qualifiers should not be used outside of the Craniata (taxid=89593)
6.56.	Qualifier	recombination_class
	Definition	a structured description of the classification of recombination hotspot region within a sequence
	Mandatory value format	TYPE where TYPE is one of the following controlled vocabulary terms or phrases: meiotic mitotic non_allelic_homologous chromosome_breakpoint other
	Example	<INSDQualifier_value>meiotic</INSDQualifier_value> <INSDQualifier_value>chromosome_breakpoint</INSDQualifier_value>
	Comment	specific recombination classes not yet in the recombination_class controlled vocabulary must be annotated by entering “other” as the recombination_class qualifier value and providing a brief explanation of the novel recombination_class

		in a note qualifier
6.57.	Qualifier	regulatory_class
	Definition	a structured description of the classification of transcriptional, translational, replicational and chromatin structure related regulatory elements in a sequence
	Mandatory value format	TYPE where TYPE is one of the following controlled vocabulary terms or phrases: attenuator CAAT_signal DNase_I_hypersensitive_site enhancer enhancer_blocking_element GC_signal imprinting_control_region insulator locus_control_region matrix_attachment_region minus_35_signal minus_10_signal polyA_signal_sequence promoter recoding_stimulatory_region recombination_enhancer replication_regulatory_region response_element ribosome_binding_site riboswitch silencer TATA_box terminator transcriptional_cis_regulatory_region uORF other
	Example	<INSDQualifier_value>promoter</INSDQualifier_value> <INSDQualifier_value>enhancer</INSDQualifier_value> <INSDQualifier_value>ribosome_binding_site</INSDQualifier_value>
	Comment	specific regulatory classes not yet in the regulatory_class controlled vocabulary must be annotated by entering “other” as the regulatory_class qualifier value and providing a brief explanation of the novel regulatory_class in a note qualifier
6.58.	Qualifier	replace
	Definition	indicates that the sequence identified in a feature’s location is replaced by the sequence shown in the qualifier’s value; if no sequence (i.e., no value) is contained within the qualifier, this indicates a deletion
	Mandatory value format	free text
	Example	<INSDQualifier_value>a</INSDQualifier_value> <INSDQualifier_value></INSDQualifier_value> - for a deletion
6.59.	Qualifier	ribosomal_slippage
	Definition	during protein translation, certain sequences can program ribosomes to change to an alternative reading frame by a mechanism known as ribosomal slippage
	Value format	none

	Comment	a join operator, e.g., [join(486..1784,1787..4810)] must be used in the CDS feature location to indicate the location of ribosomal_slippage

6.60.	Qualifier	rpt_family
	Definition	type of repeated sequence; "Alu" or "Kpn", for example
	Mandatory value format	free text
	Example	<INSDQualifier_value>Alu</INSDQualifier_value>

6.61.	Qualifier	rpt_type
	Definition	structure and distribution of repeated sequence
	Mandatory value format	One of the following controlled vocabulary terms or phrases: tandem direct inverted flanking nested terminal dispersed long_terminal_repeat non_ltr_retrotransposon_polymeric_tract centromeric_repeat telomeric_repeat x_element_combinatorial_repeat y_prime_element other
	Example	<INSDQualifier_value>inverted</INSDQualifier_value> <INSDQualifier_value>long_terminal_repeat</INSDQualifier_value>
	Comment	Definitions of the values: tandem - a repeat that exists adjacent to another in the same orientation; direct - a repeat that exists not always adjacent but is in the same orientation; inverted – a repeat pair occurring in reverse orientation to one another on the same molecule; flanking - a repeat lying outside the sequence for which it has functional significance (eg. transposon insertion target sites); nested - a repeat that is disrupted by the insertion of another element; dispersed - a repeat that is found dispersed throughout the genome; terminal - a repeat at the ends of and within the sequence for which it has functional significance (eg. transposon LTRs); long_terminal_repeat - a sequence directly repeated at both ends of a defined sequence, of the sort typically found in retroviruses; non_ltr_retrotransposon_polymeric_tract - a polymeric tract, such as poly(dA), within a non LTR retrotransposon; centromeric_repeat - a repeat region found within the modular centromere; telomeric_repeat - a repeat region found within the telomere; x_element_combinatorial_repeat - a repeat region located between the X element and the telomere or adjacent Y' element; y_prime_element - a repeat region located adjacent to telomeric repeats or X element combinatorial repeats, either as a single copy or tandem repeat of two to four copies; other - a repeat exhibiting important attributes that cannot be described by other values.

6.62.	Qualifier	rpt_unit_range
	Definition	location of a repeating unit expressed as a range
	Mandatory value format	<base_range> - where <base_range> is the first and last base (separated by two dots) of a repeating unit
	Example	<INSDQualifier_value>202..245</INSDQualifier_value>
	Comment	used to indicate the base range of the sequence that constitutes a repeating unit within the region specified by the feature keys oriT and repeat_region.

6.63.	Qualifier	rpt_unit_seq
	Definition	identity of a repeat sequence
	Mandatory value format	free text
	Example	<INSDQualifier_value>aagggc</INSDQualifier_value> <INSDQualifier_value>ag(5)tg(8)</INSDQualifier_value> <INSDQualifier_value>(AAAGA)6(AAAA)1(AAAGA)12</INSDQualifier_value>
	Comment	used to indicate the literal sequence that constitutes a repeating unit within the region specified by the feature keys oriT and repeat_region

6.64.	Qualifier	satellite
	Definition	identifier for a satellite DNA marker, composed of many tandem repeats (identical or related) of a short basic repeated unit
	Mandatory value format	<satellite_type>[:<class>][<identifier>] - where <satellite_type> is one of the following: satellite microsatellite minisatellite
	Example	<INSDQualifier_value>satellite: S1a</INSDQualifier_value> <INSDQualifier_value>satellite: alpha</INSDQualifier_value> <INSDQualifier_value>satellite: gamma III</INSDQualifier_value> <INSDQualifier_value>microsatellite: DC130</INSDQualifier_value>
	Comment	many satellites have base composition or other properties that differ from those of the rest of the genome that allows them to be identified.

6.65.	Qualifier	segment
	Definition	name of viral or phage segment sequenced
	Mandatory value format	free text
	Example	<INSDQualifier_value>6</INSDQualifier_value>

6.66.	Qualifier	serotype
	Definition	serological variety of a species characterized by its antigenic properties
	Mandatory value format	free text Language-dependent: this value may require translation for

		International/National/Regional procedures
	Example	<INSDQualifier_value>B1</INSDQualifier_value>
	Comment	used only with the source feature key; the Bacteriological Code recommends the use of the term 'serovar' instead of 'serotype' for the prokaryotes; see the International Code of Nomenclature of Bacteria (1990 Revision) Appendix 10.B "Infraspecific Terms".
6.67.	Qualifier	serovar
	Definition	serological variety of a species (usually a prokaryote) characterized by its antigenic properties
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>O157:H7</INSDQualifier_value>
	Comment	used only with the source feature key; the Bacteriological Code recommends the use of the term 'serovar' instead of 'serotype' for prokaryotes; see the International Code of Nomenclature of Bacteria (1990 Revision) Appendix 10.B "Infraspecific Terms".
6.68.	Qualifier	sex
	Definition	sex of the organism from which the sequence was obtained; sex is used for eukaryotic organisms that undergo meiosis and have sexually dimorphic gametes
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Examples	<INSDQualifier_value>female</INSDQualifier_value> <INSDQualifier_value>male</INSDQualifier_value> <INSDQualifier_value>hermaphrodite</INSDQualifier_value> <INSDQualifier_value>unisexual</INSDQualifier_value> <INSDQualifier_value>bisexual</INSDQualifier_value> <INSDQualifier_value>asexual</INSDQualifier_value> <INSDQualifier_value>monoecious</INSDQualifier_value> [or monecious] <INSDQualifier_value>dioecious</INSDQualifier_value> [or diecious]
	Comment	The sex qualifier should be used (instead of mating_type qualifier) in the Metazoa, Embryophyta, Rhodophyta & Phaeophyceae; mating_type qualifier should be used (instead of sex qualifier) in the Bacteria, Archaea & Fungi; neither sex nor mating_type qualifiers should be used in the viruses; outside of the taxa listed above, mating_type qualifier should be used unless the value of the qualifier is taken from the vocabulary given in the examples above
6.69.	Qualifier	standard_name
	Definition	accepted standard name for this feature
	Mandatory value format	free text this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>dotted</INSDQualifier_value>
	Comment	use standard_name qualifier to give full gene name, but use gene qualifier to give

		gene symbol (in the above example gene qualifier value is Dt).
6.70.	Qualifier	strain
	Definition	strain from which sequence was obtained
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>BALB/c</INSDQualifier_value>
	Comment	feature entries including a strain qualifier must not include the environmental_sample qualifier
6.71.	Qualifier	sub_clone
	Definition	sub-clone from which sequence was obtained
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>lambda-hIL7.20g</INSDQualifier_value>
	Comment	a source feature must not contain more than one sub_clone qualifier; to indicate that the sequence was obtained from multiple sub_clones, multiple sources may be further described using the feature key “misc_feature” and the qualifier “note”
6.72.	Qualifier	sub_species
	Definition	name of sub-species of organism from which sequence was obtained
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>lactis</INSDQualifier_value>
6.73.	Qualifier	sub_strain
	Definition	name or identifier of a genetically or otherwise modified strain from which sequence was obtained, derived from a parental strain (which should be annotated in the strain qualifier). sub_strain from which sequence was obtained
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>abis</INSDQualifier_value>
	Comment	must be accompanied by a strain qualifier in a source feature; if the parental strain is not given, the modified strain should be annotated in the strain qualifier instead of sub_strain. For example, either a strain qualifier with the value K-12 and a substrain qualifier with the value MG1655 or a strain qualifier with the value MG1655

6.74.	Qualifier	tag_peptide
	Definition	base location encoding the polypeptide for proteolysis tag of tmRNA and its termination codon
	Mandatory value format	<base_range> - where <base_range> provides the first and last base (separated by two dots) of the location for the proteolysis tag
	Example	<INSDQualifier_value>90..122</INSDQualifier_value>
	Comment	it is recommended that the amino acid sequence corresponding to the tag_peptide be annotated by describing a 5' partial CDS feature; e.g., CDS with a location of <90..122

6.75.	Qualifier	tissue_lib
	Definition	tissue library from which sequence was obtained
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>tissue library 772</INSDQualifier_value>

6.76.	Qualifier	tissue_type
	Definition	tissue type from which the sequence was obtained
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>liver</INSDQualifier_value>

6.77.	Qualifier	transl_except
	Definition	translational exception: single codon the translation of which does not conform to genetic code defined by organism or transl_table.
	Mandatory value format	(pos:<location>,aa:<amino_acid>) where <amino_acid> is the three letter abbreviation for the amino acid coded by the codon at the base_range position
	Example	<INSDQualifier_value>(pos:213..215,aa:Trp)</INSDQualifier_value> <INSDQualifier_value>(pos:462..464,aa:OTHER)</INSDQualifier_value> <INSDQualifier_value>(pos:1017,aa:TERM)</INSDQualifier_value> <INSDQualifier_value>(pos:2000..2001,aa:TERM)</INSDQualifier_value>
	Comment	if the amino acid is not one of the specific amino acids listed in Section 3 of this Annex, use OTHER as <amino_acid> and provide the name of the unusual amino acid in a note qualifier; for modified amino-acid selenocysteine use three letter abbreviation 'Sec' (one letter symbol 'U' in amino-acid sequence) for <amino_acid>; for modified amino-acid pyrrolysine use three letter abbreviation 'Pyl' (one letter symbol 'O' in amino-acid sequence) for <amino _acid>; for partial termination codons where TAA stop codon is completed by the addition of 3' A residues to the mRNA either a single base_position or a base_range is used for the location, see the third and fourth examples above, in conjunction with a note qualifier indicating 'stop codon completed by the addition of 3' A residues to the mRNA'.

6.78.	Qualifier	transl_table
	Definition	definition of genetic code table used if other than universal or standard genetic code table. Tables used are described in this Annex
	Mandatory value format	<integer> where <integer> is the number assigned to the genetic code table
	Example	<INSDQualifier_value>3</INSDQualifier_value> - example where the yeast mitochondrial code is to be used
	Comment	if the transl_table qualifier is not used to further annotate a CDS feature key, then the CDS is translated using the Standard Code (i.e. Universal Genetic Code). Genetic code exceptions outside the range of specified tables are reported in transl_except qualifiers.
6.79.	Qualifier	trans_splicing
	Definition	indicates that exons from two RNA molecules are ligated in intermolecular reaction to form mature RNA
	Value format	none
	Comment	should be used on features such as CDS, mRNA and other features that are produced as a result of a trans-splicing event. This qualifier must be used only when the splice event is indicated in the "join" operator, e.g., join(complement(69611..69724),139856..140087) in the feature location
6.80.	Qualifier	translation
	Definition	one-letter abbreviated amino acid sequence derived from either the standard (or universal) genetic code or the table as specified in a transl_table qualifier and as determined by an exception in the transl_except qualifier
	Mandatory value format	contiguous string of one-letter amino acid abbreviations from Section 3 of this Annex, "X" is to be used for AA exceptions.
	Example	<INSDQualifier_value>MASTFPPWYRGCASTPSLKGLIMCTW</INSDQualifier_value>
	Comment	to be used with CDS feature only; must be accompanied by protein_id qualifier when the translation product contains four or more specifically defined amino acids; see transl_table for definition and location of genetic code Tables; only one of the qualifiers translation, pseudo and pseudogene are permitted to further annotate a CDS feature.
6.81.	Qualifier	variety
	Definition	variety (= varietas, a formal Linnaean rank) of organism from which sequence was derived.
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>insularis</INSDQualifier_value>
	Comment	use the cultivar qualifier for cultivated plant varieties, i.e., products of artificial selection; varieties other than plant and fungal variatas should be annotated via a note qualifier, e.g., with the value <INSDQualifier_value>breed:Cukorova</INSDQualifier_value>

SECTION 7: FEATURE KEYS FOR AMINO ACID SEQUENCES

This section contains the list of allowed feature keys to be used for amino acid sequences. The feature keys are listed in alphabetic order.

7.1.	Feature Key	ACT_SITE
	Definition	Amino acid(s) involved in the activity of an enzyme
	Optional qualifiers	note
	Comment	Each amino acid residue of the active site must be annotated separately with the ACT_SITE feature key. The corresponding amino acid residue number must be provided as the location descriptor in the feature location element.

7.2.	Feature Key	BINDING
	Definition	Binding site for any chemical group (co-enzyme, prosthetic group, etc.). The chemical nature of the group is indicated in the note qualifier
	Mandatory qualifiers	note
	Comment	Examples of values for the “note” qualifier: “Heme (covalent)” and “Chloride.” Where appropriate, the features keys CA_BIND, DNA_BIND, METAL, and NP_BIND should be used rather than BINDING.

7.3.	Feature Key	CA_BIND
	Definition	Extent of a calcium-binding region
	Optional qualifiers	note

7.4.	Feature Key	CARBOHYD
	Definition	Glycosylation site
	Mandatory qualifiers	note
	Comment	This key describes the occurrence of the attachment of a glycan (mono- or polysaccharide) to a residue of the protein. The type of linkage (C-, N- or O-linked) to the protein is indicated in the “note” qualifier. If the nature of the reducing terminal sugar is known, its abbreviation is shown between parentheses. If three dots ’...’ follow the abbreviation this indicates an extension of the carbohydrate chain. Conversely no dots means that a monosaccharide is linked. Examples of values used in the “note” qualifier: N-linked (GlcNAc...); O-linked (GlcNAc); O-linked (Glc...); C-linked (Man) partial; O-linked (Ara...).

7.5.	Feature Key	CHAIN
	Definition	Extent of a polypeptide chain in the mature protein
	Optional qualifiers	note

7.6.	Feature Key	COILED
	Definition	Extent of a coiled-coil region
	Optional qualifiers	note

7.7.	Feature Key	COMPBIAS
	Definition	Extent of a compositionally biased region
	Optional qualifiers	note

7.8.	Feature Key	CONFLICT
	Definition	Different sources report differing sequences
	Optional qualifiers	note
	Comment	Examples of values for the “note” qualifier: Missing; K -> Q; GSDSE -> RIRLR; V -> A.

7.9.	Feature Key	CROSSLNK
	Definition	Post translationally formed amino acid bonds
	Mandatory qualifiers	note
	Comment	Covalent linkages of various types formed between two proteins (interchain cross-links) or between two parts of the same protein (intrachain cross-links); except for cross-links formed by disulfide bonds, for which the “DISULFID” feature key is to be used. For an interchain cross-link, the location descriptor in the feature location element is the residue number of the amino acid cross-linked to the other protein. For an intrachain cross-link, the location descriptor in the feature location element is the residue numbers of the cross-linked amino acids in “x..y” format, e.g. “42..50”. The note qualifier indicates the nature of the cross-link; at least specifying the name of the conjugate and the identity of the two amino acids involved. Examples of values for the “note” qualifier: “Isoglutamyl cysteine thioester (Cys-Gln);” “Beta-methyllanthionine (Cys-Thr);” and “Glycyl lysine isopeptide (Lys-Gly) (interchain with G-Cter in ubiquitin)”

7.10.	Feature Key	DISULFID
	Definition	Disulfide bond
	Mandatory qualifiers	note
	Comment	For an interchain disulfide bond, the location descriptor in the feature location element is the residue number of the cysteine linked to the other protein. For an intrachain cross-link, the location descriptor in the feature location element is the residue numbers of the linked cysteines in “x..y” format, e.g. “42..50”. For interchain disulfide bonds, the note qualifier indicates the nature of the cross-link, by identifying the other protein, for example, “Interchain (between A and B chains)”

7.11.	Feature Key	DNA_BIND
	Definition	Extent of a DNA-binding region

	Mandatory qualifiers	note
	Comment	The nature of the DNA-binding region is given in the note qualifier. Examples of values for the “note” qualifier: “Homeobox” and “Myb 2”

7.12.	Feature Key	DOMAIN
	Definition	Extent of a domain, which is defined as a specific combination of secondary structures organized into a characteristic three-dimensional structure or fold
	Mandatory qualifiers	note
	Comment	The domain type is given in the note qualifier. Where several copies of a domain are present, the domains are numbered. Examples of values for the “note” qualifier: “Ras-GAP” and “Cadherin 1”

7.13.	Feature Key	HELIX
	Definition	Secondary structure: Helices, for example, Alpha-helix; 3(10) helix; or Pi-helix
	Optional qualifiers	note
	Comment	This feature is used only for proteins whose tertiary structure is known. Only three types of secondary structure are specified: helices (key HELIX), beta-strands (key STRAND) and turns (key TURN). Residues not specified in one of these classes are in a ’loop’ or ’random-coil’ structure.

7.14.	Feature Key	INIT_MET
	Definition	Initiator methionine
	Optional qualifiers	note
	Comment	The location descriptor in the feature location element is “1”. This feature key indicates the N-terminal methionine is cleaved off. This feature is not used when the initiator methionine is not cleaved off.

7.15.	Feature Key	INTRAMEM
	Definition	Extent of a region located in a membrane without crossing it
	Optional qualifiers	note

7.16.	Feature Key	LIPID
	Definition	Covalent binding of a lipid moiety
	Mandatory qualifiers	note
	Comment	The chemical nature of the bound lipid moiety is given in the note qualifier, indicating at least the name of the lipidated amino acid. Examples of values for the “note” qualifier: “N-myristoyl glycine”; “GPI-anchor amidated serine” and “S-diacylglycerol cysteine.”

7.17.	Feature Key	METAL
	Definition	Binding site for a metal ion.
	Mandatory qualifiers	note
	Comment	The note qualifier indicates the nature of the metal. Examples of values for the "note" qualifier: "Iron (heme axial ligand)" and "Copper".

7.18.	Feature Key	MOD_RES
	Definition	Posttranslational modification of a residue
	Mandatory qualifiers	note
	Comment	The chemical nature of the modified residue is given in the note qualifier, indicating at least the name of the post-translationally modified amino acid. If the modified amino acid is listed in Section 4 of this Annex, the abbreviation may be used in place of the the full name. Examples of values for the "note" qualifier: "N-acetylalanine"; "3-Hyp"; and "MeLys" or "N-6-methyllysine"

7.19.	Feature Key	MOTIF
	Definition	Short (up to 20 amino acids) sequence motif of biological interest
	Optional qualifiers	note

7.20.	Feature Key	MUTAGEN
	Definition	Site which has been experimentally altered by mutagenesis
	Optional qualifiers	note

7.21.	Feature Key	NON_STD
	Definition	Non-standard amino acid
	Optional qualifiers	note
	Comment	This key only describes the occurrence of non-standard amino acids selenocysteine (U) and pyrrolysine (O) in the amino acid sequence.

7.22.	Feature Key	NON_TER
	Definition	The residue at an extremity of the sequence is not the terminal residue
	Optional qualifiers	note
	Comment	If applied to position 1, this means that the first position is not the N-terminus of the complete molecule. If applied to the last position, it means that this position is not the C-terminus of the complete molecule.

7.23.	Feature Key	NP_BIND
	Definition	Extent of a nucleotide phosphate-binding region
	Mandatory qualifiers	note
	Comment	The nature of the nucleotide phosphate is indicated in the note qualifier. Examples of values for the “note” qualifier: “ATP” and “FAD”.

7.24.	Feature Key	PEPTIDE
	Definition	Extent of a released active peptide
	Optional qualifiers	note

7.25.	Feature Key	PROPEP
	Definition	Extent of a propeptide
	Optional qualifiers	note

7.26.	Feature Key	REGION
	Definition	Extent of a region of interest in the sequence
	Optional qualifiers	note

7.27.	Feature Key	REPEAT
	Definition	Extent of an internal sequence repetition
	Optional qualifiers	note

7.28.	Feature Key	SIGNAL
	Definition	Extent of a signal sequence (prepeptide)
	Optional qualifiers	note

7.29.	Feature Key	SITE
	Definition	Any interesting single amino-acid site on the sequence that is not defined by another feature key. It can also apply to an amino acid bond which is represented by the positions of the two flanking amino acids
	Mandatory qualifier	note
	Comment	When SITE is used to annotate a modified amino acid the value for the qualifier “note” must either be an abbreviation set forth in Section 4 of this Annex, or the complete, unabbreviated name of the modified amino acid.

7.30.	Feature Key	source
	Definition	Identifies the source of the sequence; this key is mandatory; every sequence will have a single source feature spanning the entire sequence
	Mandatory qualifiers	mol_type organism
	Optional qualifiers	note

7.31.	Feature Key	STRAND
	Definition	Secondary structure: Beta-strand; for example Hydrogen bonded beta-strand or residue in an isolated beta-bridge
	Optional qualifiers	note
	Comment	This feature is used only for proteins whose tertiary structure is known. Only three types of secondary structure are specified: helices (key HELIX), beta-strands (key STRAND) and turns (key TURN). Residues not specified in one of these classes are in a 'loop' or 'random-coil' structure.

7.32.	Feature Key	TOPO_DOM
	Definition	Topological domain
	Optional qualifiers	note

7.33.	Feature Key	TRANSMEM
	Definition	Extent of a transmembrane region
	Optional qualifiers	note

7.34.	Feature Key	TRANSIT
	Definition	Extent of a transit peptide (mitochondrion, chloroplast, thylakoid, cyanelle, peroxisome etc.)
	Optional qualifiers	note

7.35.	Feature Key	TURN
	Definition	Secondary structure Turns, for example, H-bonded turn (3-turn, 4-turn or 5-turn)
	Optional qualifiers	note
	Comment	This feature is used only for proteins whose tertiary structure is known. Only three types of secondary structure are specified: helices (key HELIX), beta-strands (key STRAND) and turns (key TURN). Residues not specified in one of these classes are in a 'loop' or 'random-coil' structure.

7.36.	Feature Key	UNSURE
	Definition	Uncertainties in the sequence
	Optional qualifiers	note
	Comment	Used to describe region(s) of an amino acid sequence for which the authors are unsure about the sequence presentation.

7.37.	Feature Key	VARIANT
	Definition	Authors report that sequence variants exist
	Optional qualifiers	note

7.38.	Feature Key	VAR_SEQ
	Definition	Description of sequence variants produced by alternative splicing, alternative promoter usage, alternative initiation and ribosomal frameshifting
	Optional qualifiers	note

7.39.	Feature Key	ZN_FING
	Definition	Extent of a zinc finger region
	Mandatory qualifiers	note
	Comment	The type of zinc finger is indicated in the note qualifier. For example: “GATA-type” and “NR C4-type”

SECTION 8: QUALIFIERS FOR AMINO ACID SEQUENCES

This section contains the list of allowed qualifiers to be used for amino acid sequences.

Where the value format is free text that is identified as language-dependent, one of the following must be used:

1) the `INSDQualifier_value` element; or
2) the `NonEnglishQualifier_value` element; or
3) both the `INSDQualifier_value` element and the `NonEnglishQualifier_value` element.

Where the value format is not identified as language-dependent free text, the `INSDQualifier_value` element must be used and the `NonEnglishQualifier_value` element must not be used.

PLEASE NOTE: Any qualifier value provided for a qualifier with a language-dependent free text value format may require translation for international, national or regional procedures. The qualifiers listed in the following table are considered to have language-dependent free text values:

Table 6: List of qualifiers with language-dependent free text values for amino acid sequences

Section	Language-Dependent Free Text Qualifier
8.2	note
8.3	organism

8.1.	Qualifier	mol_type
	Definition	In vivo molecule type of sequence
	Mandatory value format	protein
	Example	<INSDQualifier_value>protein</INSDQualifier_value>
	Comment	The "mol_type" qualifier is mandatory on the source feature key.

8.2.	Qualifier	note
	Definition	Any comment or additional information
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>Heme (covalent)</INSDQualifier_value>
	Comment	The “note” qualifier is mandatory for the feature keys: BINDING; CARBOHYD; CROSSLNK; DISULFID; DNA_BIND; DOMAIN; LIPID; METAL; MOD_RES; NP_BIND; SITE and ZN_FING

8.3.	Qualifier	organism
	Definition	Scientific name of the organism that provided the peptide
	Mandatory value format	free text Language-dependent: this value may require translation for International/National/Regional procedures
	Example	<INSDQualifier_value>Homo sapiens</INSDQualifier_value>
	Comment	The “organism” qualifier is mandatory for the source feature key.

SECTION 9: GENETIC CODE TABLES

Table 7 reproduces Genetic Code Tables to be used for translating coding sequences. The value for the trans_table qualifier is the number assigned to the corresponding genetic code table. Where a CDS feature is described with a translation qualifier but not a transl_table qualifier, the 1 - Standard Code is used by default for translation. (Note: Genetic code tables 7, 8, 15, and 17 to 20 do not exist, therefore these numbers do not appear in Table 7.)

Table 7: Genetic Code Tables

1 - Standard Code
AAs = FFLLSSSSYY**CC*WLLLLPPPPHHQQRRRRIIIMTTTTNNKKSSRRVVVVAAAADDEEGGGG Starts = ---M---------------M---------------M---------------------------- Base1 = TTTTTTTTTTTTTTTTCCCCCCCCCCCCCCCCAAAAAAAAAAAAAAAAGGGGGGGGGGGGGGGG Base2 = TTTTCCCCAAAAGGGGTTTTCCCCAAAAGGGGTTTTCCCCAAAAGGGGTTTTCCCCAAAAGGGG Base3 = TCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAG
2 - Vertebrate Mitochondrial Code
AAs = FFLLSSSSYY**CCWWLLLLPPPPHHQQRRRRIIMMTTTTNNKKSS**VVVVAAAADDEEGGGG Starts = --------------------------------MMMM---------------M------------ Base1 = TTTTTTTTTTTTTTTTCCCCCCCCCCCCCCCCAAAAAAAAAAAAAAAAGGGGGGGGGGGGGGGG Base2 = TTTTCCCCAAAAGGGGTTTTCCCCAAAAGGGGTTTTCCCCAAAAGGGGTTTTCCCCAAAAGGGG Base3 = TCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAG
3 - Yeast Mitochondrial Code
AAs = FFLLSSSSYY**CCWWTTTTPPPPHHQQRRRRIIMMTTTTNNKKSSRRVVVVAAAADDEEGGGG Starts = ----------------------------------MM----------------M------------ Base1 = TTTTTTTTTTTTTTTTCCCCCCCCCCCCCCCCAAAAAAAAAAAAAAAAGGGGGGGGGGGGGGGG Base2 = TTTTCCCCAAAAGGGGTTTTCCCCAAAAGGGGTTTTCCCCAAAAGGGGTTTTCCCCAAAAGGGG Base3 = TCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAG
4 - Mold, Protozoan, Coelenterate Mitochondrial Code & Mycoplasma/Spiroplasma Code
AAs = FFLLSSSSYY**CCWWLLLLPPPPHHQQRRRRIIIMTTTTNNKKSSRRVVVVAAAADDEEGGGG Starts = --MM---------------M------------MMMM---------------M------------ Base1 = TTTTTTTTTTTTTTTTCCCCCCCCCCCCCCCCAAAAAAAAAAAAAAAAGGGGGGGGGGGGGGGG Base2 = TTTTCCCCAAAAGGGGTTTTCCCCAAAAGGGGTTTTCCCCAAAAGGGGTTTTCCCCAAAAGGGG Base3 = TCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAG
5 - Invertebrate Mitochondrial Code
AAs = FFLLSSSSYY**CCWWLLLLPPPPHHQQRRRRIIMMTTTTNNKKSSSSVVVVAAAADDEEGGGG Starts = ---M------------------------------MMMM---------------M------------ Base1 = TTTTTTTTTTTTTTTTCCCCCCCCCCCCCCCCAAAAAAAAAAAAAAAAGGGGGGGGGGGGGGGG Base2 = TTTTCCCCAAAAGGGGTTTTCCCCAAAAGGGGTTTTCCCCAAAAGGGGTTTTCCCCAAAAGGGG Base3 = TCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAG
6 - Ciliate, Dasycladacean and Hexamita Nuclear Code
AAs = FFLLSSSSYYQQCC*WLLLLPPPPHHQQRRRRIIIMTTTTNNKKSSRRVVVVAAAADDEEGGGG Starts = ----------------------------------M---------------------------- Base1 = TTTTTTTTTTTTTTTTCCCCCCCCCCCCCCCCAAAAAAAAAAAAAAAAGGGGGGGGGGGGGGGG Base2 = TTTTCCCCAAAAGGGGTTTTCCCCAAAAGGGGTTTTCCCCAAAAGGGGTTTTCCCCAAAAGGGG Base3 = TCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAG

9 - Echinoderm and Flatworm Mitochondrial Code

```
  AAs  =  FFLLSSSSYY**CCWWLLLLPPPPHHQQRRRRIIIMTTTTNNNKSSSSVVVVAAAADDEEGGGG
Starts =  ----------------------------------M---------------M------------
Base1  =  tttttttttttttttcccccccccccccccaaaaaaaaaaaaaaaaggggggggggggggggg
Base2  =  ttttccccaaaaggggttttccccaaaaggggttttccccaaaaggggttttccccaaaagggg
Base3  =  tcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcag
```

10 - Euplotid Nuclear Code

```
  AAs  =  FFLLSSSSYY**CCCWLLLLPPPPHHQQRRRRIIIMTTTTNNKKSSRRVVVVAAAADDEEGGGG
Starts =  ----------------------------------M----------------------------
Base1  =  tttttttttttttttcccccccccccccccaaaaaaaaaaaaaaaaggggggggggggggggg
Base2  =  ttttccccaaaaggggttttccccaaaaggggttttccccaaaaggggttttccccaaaagggg
Base3  =  tcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcag
```

11 – Bacterial, Archaeal, and Plant Plastid Code

```
  AAs  =  FFLLSSSSYY**CC*WLLLLPPPPHHQQRRRRIIIMTTTTNNKKSSRRVVVVAAAADDEEGGGG
Starts =  ---M---------------M------------MMMM---------------M------------
Base1  =  tttttttttttttttcccccccccccccccaaaaaaaaaaaaaaaaggggggggggggggggg
Base2  =  ttttccccaaaaggggttttccccaaaaggggttttccccaaaaggggttttccccaaaagggg
Base3  =  tcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcag
```

12 - Alternative Yeast Nuclear Code

```
  AAs  =  FFLLSSSSYY**CC*WLLLSPPPPHHQQRRRRIIIMTTTTNNKKSSRRVVVVAAAADDEEGGGG
Starts =  -------------------M---------------M----------------------------
Base1  =  tttttttttttttttcccccccccccccccaaaaaaaaaaaaaaaaggggggggggggggggg
Base2  =  ttttccccaaaaggggttttccccaaaaggggttttccccaaaaggggttttccccaaaagggg
Base3  =  tcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcag
```

13 - Ascidian Mitochondrial Code

```
  AAs  =  FFLLSSSSYY**CCWWLLLLPPPPHHQQRRRRIIMMTTTTNNKKSSGGVVVVAAAADDEEGGGG
Starts =  ---M------------------------------MM---------------M------------
Base1  =  tttttttttttttttcccccccccccccccaaaaaaaaaaaaaaaaggggggggggggggggg
Base2  =  ttttccccaaaaggggttttccccaaaaggggttttccccaaaaggggttttccccaaaagggg
Base3  =  tcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcag
```

14 - Alternative Flatworm Mitochondrial Code

```
  AAs  =  FFLLSSSSYYY*CCWWLLLLPPPPHHQQRRRRIIIMTTTTNNNKSSSSVVVVAAAADDEEGGGG
Starts =  ----------------------------------M----------------------------
Base1  =  tttttttttttttttcccccccccccccccaaaaaaaaaaaaaaaaggggggggggggggggg
Base2  =  ttttccccaaaaggggttttccccaaaaggggttttccccaaaaggggttttccccaaaagggg
Base3  =  tcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcag
```

16 - Chlorophycean Mitochondrial Code

```
  AAs  =  FFLLSSSSYY*LCC*WLLLLPPPPHHQQRRRRIIIMTTTTNNKKSSRRVVVVAAAADDEEGGGG
Starts =  ----------------------------------M----------------------------
Base1  =  tttttttttttttttcccccccccccccccaaaaaaaaaaaaaaaaggggggggggggggggg
Base2  =  ttttccccaaaaggggttttccccaaaaggggttttccccaaaaggggttttccccaaaagggg
Base3  =  tcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcag
```

21 - Trematode Mitochondrial Code

```
  AAs  =  FFLLSSSSYY**CCWWLLLLPPPPHHQQRRRRIIMMTTTTNNNKSSSSVVVVAAAADDEEGGGG
Starts =  ----------------------------------M---------------M------------
Base1  =  tttttttttttttttcccccccccccccccaaaaaaaaaaaaaaaaggggggggggggggggg
Base2  =  ttttccccaaaaggggttttccccaaaaggggttttccccaaaaggggttttccccaaaagggg
Base3  =  tcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcag
```

22 - Scenedesmus obliquus Mitochondrial Code

```
  AAs  =  FFLLSS*SYY*LCC*WLLLLPPPPHHQQRRRRIIIMTTTTNNKKSSRRVVVVAAAADDEEGGGG
Starts =  ----------------------------------M-----------------------------
Base1  =  tttttttttttttttcccccccccccccccaaaaaaaaaaaaaaaaggggggggggggggggg
Base2  =  ttttccccaaaaggggttttccccaaaaggggttttccccaaaaggggttttccccaaaagggg
Base3  =  tcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcag
```

23 - Thraustochytrium Mitochondrial Code

```
  AAs  =  FF*LSSSSYY**CC*WLLLLPPPPHHQQRRRRIIIMTTTTNNKKSSRRVVVVAAAADDEEGGGG
Starts =  --------------------------------M--M---------------M------------
Base1  =  tttttttttttttttcccccccccccccccaaaaaaaaaaaaaaaaggggggggggggggggg
Base2  =  ttttccccaaaaggggttttccccaaaaggggttttccccaaaaggggttttccccaaaagggg
Base3  =  tcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcag
```

24 - Pterobranchia Mitochondrial Code

```
  AAs  =  FFLLSSSSYY**CCWWLLLLPPPPHHQQRRRRIIIMTTTTNNKKSSSKVVVVAAAADDEEGGGG
Starts =  ---M---------------M---------------M---------------M------------
Base1  =  tttttttttttttttcccccccccccccccaaaaaaaaaaaaaaaaggggggggggggggggg
Base2  =  ttttccccaaaaggggttttccccaaaaggggttttccccaaaaggggttttccccaaaagggg
Base3  =  tcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcag
```

25 - Candidate Division SR1 and Gracilibacteria Code

```
  AAs  = FFLLSSSSYY**CCGWLLLLPPPPHHQQRRRRIIIMTTTTNNKKSSRRVVVVAAAADDEEGGGG
Starts = ---M------------------------------M---------------M------------
Base1  = tttttttttttttttcccccccccccccccaaaaaaaaaaaaaaaaggggggggggggggggg
Base2  = ttttccccaaaaggggttttccccaaaaggggttttccccaaaaggggttttccccaaaagggg
Base3  = tcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcag
```

26 - Pachysolen tannophilus Nuclear Code

```
  AAs  = FFLLSSSSYY**CC*WLLLAPPPPHHQQRRRRIIIMTTTTNNKKSSRRVVVVAAAADDEEGGGG
Starts = --------------------M---------------M-----------------------------
Base1  = tttttttttttttttcccccccccccccccaaaaaaaaaaaaaaaaggggggggggggggggg
Base2  = ttttccccaaaaggggttttccccaaaaggggttttccccaaaaggggttttccccaaaagggg
Base3  = tcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcag
```

27 - Karyorelict Nuclear Code

```
  AAs  =  FFLLSSSSYYQQCCWWLLLLPPPPHHQQRRRRIIIMTTTTNNKKSSRRVVVVAAAADDEEGGGG
Starts =  ---------------*--------------------M-----------------------------
Base1  =  tttttttttttttttcccccccccccccccaaaaaaaaaaaaaaaaggggggggggggggggg
Base2  =  ttttccccaaaaggggttttccccaaaaggggttttccccaaaaggggttttccccaaaagggg
Base3  =  tcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcag
```

28 - Condylostoma Nuclear Code

```
  AAs  =  FFLLSSSSYYQQCCWWLLLLPPPPHHQQRRRRIIIMTTTTNNKKSSRRVVVVAAAADDEEGGGG
Starts =  ----------**--*--------------------M----------------------------
Base1  =  tttttttttttttttcccccccccccccccaaaaaaaaaaaaaaaaggggggggggggggggg
Base2  =  ttttccccaaaaggggttttccccaaaaggggttttccccaaaaggggttttccccaaaaggggg
Base3  =  tcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcag
```

29 - Mesodinium Nuclear Code

```
  AAs  =  FFLLSSSSYYYYCC*WLLLLPPPPHHQQRRRRIIIMTTTTNNKKSSRRVVVVAAAADDEEGGGG
Starts =  -----------------------------------M----------------------------
Base1  =  tttttttttttttttcccccccccccccccaaaaaaaaaaaaaaaaggggggggggggggggg
Base2  =  ttttccccaaaaggggttttccccaaaaggggttttccccaaaaggggttttccccaaaaggggg
Base3  =  tcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcag
```

30 - Peritrich Nuclear Code

```
  AAs  =  FFLLSSSSYYEECC*WLLLLPPPPHHQQRRRRIIIMTTTTNNKKSSRRVVVVAAAADDEEGGGG
Starts =  -----------------------------------M----------------------------
Base1  =  tttttttttttttttcccccccccccccccaaaaaaaaaaaaaaaaggggggggggggggggg
Base2  =  ttttccccaaaaggggttttccccaaaaggggttttccccaaaaggggttttccccaaaaggggg
Base3  =  tcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcag
```

31 - Blastocrithidia Nuclear Code

```
  AAs  =  FFLLSSSSYYEECCWWLLLLPPPPHHQQRRRRIIIMTTTTNNKKSSRRVVVVAAAADDEEGGGG
Starts =  ----------**----------------------M----------------------------
Base1  =  tttttttttttttttcccccccccccccccaaaaaaaaaaaaaaaaggggggggggggggggg
Base2  =  ttttccccaaaaggggttttccccaaaaggggttttccccaaaaggggttttccccaaaaggggg
Base3  =  tcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcag
```

33 - Cephalodiscidae Mitochondrial UAA-Tyr Code

```
  AAs  =  FFLLSSSSYYY*CCWWLLLLPPPPHHQQRRRRIIIMTTTTNNKKSSSKVVVVAAAADDEEGGGG
Starts =  ---M---------------M---------------M---------------M------------
Base1  =  tttttttttttttttcccccccccccccccaaaaaaaaaaaaaaaaggggggggggggggggg
Base2  =  ttttccccaaaaggggttttccccaaaaggggttttccccaaaaggggttttccccaaaaggggg
Base3  =  tcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcagtcag
```

[Annex II follows]

ANNEX II

DOCUMENT TYPE DEFINITION (DTD) FOR SEQUENCE LISTING

Version 1.3

Revision approved by the Committee on WIPO Standards (CWS)
at its eleventh session on December 8, 2023

```
<?xml version="1.0" encoding="UTF-8"?>
<!--Annex II of WIPO Standard ST.26, Document Type Definition (DTD) for Sequence Listing

This entity may be identified by the PUBLIC identifier:
************************************************************************************************
PUBLIC "-//WIPO//DTD SEQUENCE LISTING 1.3//EN" "ST26SequenceListing_V1_3.dtd"
************************************************************************************************
* PUBLIC DTD URL

* https://www.wipo.int/standards/dtd/ST26SequenceListing_V1_3.dtd
************************************************************************************

************************************************************************************
* CONTACTS
************************************************************************************
standards@wipo.int

************************************************************************************
* NOTES
************************************************************************************
The sequence data part is a subset of the complete INSDC DTD V.1.5 that only covers
the requirements of WIPO Standard ST.26.

************************************************************************************
* REVISION HISTORY
************************************************************************************
2022-11-25: Revised Version 1.3 approved at CWS/10 (small edits to the comments for fileName) -
comments only so no update to version number
2021-11-05: Revised Version 1.3 approved at CWS/9 (small edits to the comments for
InventorNameLatin, INSDSeq_division, INSDSeq_feature-table) - comments only so no update to version
number
2020-05-20: Version 1.3 approved at CWS/8.
Changes:
- Optional originalFreeTextLanguageCode attribute added to <ST26SequenceListing> to allow applicants
to indicate the language of the free text in the original sequence listing.
- Optional nonEnglishFreeTextLanguageCode attribute added to <ST26SequenceListing> to allow
applicants to indicate the language of the free text provided in the element
<NonEnglishQualifier_value>.
- Optional id attribute added to INSDQualifier to facilitate comparison of language-dependent
qualifier values between sequence listings.
- Optional element <NonEnglishQualifier_value> added to element <INSDQualifier> to allow applicants
to type language-dependent qualifiers in a non-English Language with the characters set forth in
paragraph 40(a) of the ST.26 main body document.

2018-10-19: Version 1.2 approved at CWS/6.
Changes:
<INSDQualifier*> changed to <INSDQualifier+> for alignment with business needs and advice from NCBI
(an INSDFeature_quals element (if present) should have one or more INSDQualifier elements).

2017-06-02: Version 1.1 approved at the CWS/5
```

```
Changes:
Comments added to <INSDSeq_length>, <INSDSeq_division> and <INSDSeq_sequence> to clarify the reason
of the differences between the INSDC DTD v.1.5 and ST26 Sequence Listing DTD V1_1.
**************************************************************************
2016-03-24: Version 1.0 adopted at the CWS/4Bis
2014-03-11: Final draft for adoption.
**************************************************************************

ST26SequenceListing
**************************************************************************
* ROOT ELEMENT
**************************************************************************
-->
<!ELEMENT ST26SequenceListing ((ApplicantFileReference | (ApplicationIdentification,
ApplicantFileReference?)), EarliestPriorityApplicationIdentification?, (ApplicantName,
ApplicantNameLatin?)?, (InventorName, InventorNameLatin?)?, InventionTitle+, SequenceTotalQuantity,
SequenceData+)>
<!--The elements ApplicantName and InventorName are optional in this DTD to facilitate
the conversion between various encoding schemes-->
<!--originalFreeTextLanguageCode:
The language code (see reference in paragraph 9 to ISO 639-1:2002) for the single original language
in which the language-dependent free text qualifiers (NonEnglishQualifier_value) were prepared.
-->
<!--nonEnglishFreeTextLanguageCode:
The language code (see reference in paragraph 9 to ISO 639-1:2002) for the language in which the
language-dependent free text qualifiers (NonEnglishQualifier_value) currently correspond.
-->
<!-- fileName:
By default this will be set to the value provided for the project name in WIPO Sequence. If the
value is identical to
the actual ST.26 XML filename, it should be noted that Offices may enforce their requirements for
the filename used which may restrict which characters are allowable for
submitted electronic files. It is also acceptable for the value of the filename attribute and the
actual file name to be different. Please refer to the WIPO Sequence and ST.26
Knowledge Base for further details on Offices' naming conventions for electronic files  -->
<!ATTLIST ST26SequenceListing
               dtdVersion CDATA #REQUIRED
               fileName CDATA #IMPLIED
               softwareName CDATA #IMPLIED
               softwareVersion CDATA #IMPLIED
               productionDate CDATA #IMPLIED
               originalFreeTextLanguageCode CDATA #IMPLIED
               nonEnglishFreeTextLanguageCode CDATA #IMPLIED
>

<!--ApplicantFileReference
Applicant's or agent's file reference, mandatory if application identification not provided.
-->
<!ELEMENT ApplicantFileReference (#PCDATA)>
<!--ApplicationIdentification
Application identification for which the sequence listing is submitted, when available.
-->
<!ELEMENT ApplicationIdentification (IPOfficeCode, ApplicationNumberText, FilingDate?)>
<!--EarliestPriorityApplicationIdentification
Identification of the earliest priority application, which contains IPOfficeCode,
ApplicationNumberText and FilingDate elements.
-->
<!ELEMENT EarliestPriorityApplicationIdentification (IPOfficeCode, ApplicationNumberText,
FilingDate?)>
<!--ApplicantName
The name of the first mentioned applicant in characters set forth in paragraph 40(a) of the ST.26
main body document.
-->
```

```
<!--languageCode: Appropriate language code from ISO 639-1-Codes for the representation of names of
languages - Part 1: Alpha-2
-->
<!ELEMENT ApplicantName (#PCDATA)>
<!ATTLIST ApplicantName
              languageCode CDATA #REQUIRED
>
<!--ApplicantNameLatin
Where ApplicantName is typed in characters other than those as set forth in paragraph 40(b), a
translation or transliteration of the name of the first mentioned applicant must also be typed in
characters as set forth in paragraph 40(b) of the ST.26 main body document.
-->
<!ELEMENT ApplicantNameLatin (#PCDATA)>
<!--InventorName
Name of the first mentioned inventor typed in the characters as set forth in paragraph 40(a).-->
<!--languageCode: Appropriate language code from ISO 639-1-Codes for the representation of names of
languages - Part 1: Alpha-2
-->
<!ELEMENT InventorName (#PCDATA)>
<!ATTLIST InventorName
              languageCode CDATA #REQUIRED
>
<!--InventorNameLatin
Where InventorName is typed in characters other than those as set forth in paragraph 40(b), a
translation or transliteration of the first mentioned inventor may also be typed in characters as
set forth in paragraph 40(b).
-->
<!ELEMENT InventorNameLatin (#PCDATA)>
<!--InventionTitle
Title of the invention typed in the characters as set forth in paragraph 40(a) in the language of
filing. A translation of the title of the invention into additional languages may be typed in the
characters as set forth in paragraph 40(a) using additional InventionTitle elements. Preferably two
to seven words.
-->
<!--languageCode: Appropriate language code from ISO 639-1 - Codes
for the representation of names of languages - Part 1: Alpha-2
-->
<!ELEMENT InventionTitle (#PCDATA)>
<!ATTLIST InventionTitle
              languageCode CDATA #REQUIRED
>
<!--SequenceTotalQuantity
Indicates the total number of sequences in the document.
Its purpose is to be quickly accessible for automatic processing.
-->
<!ELEMENT SequenceTotalQuantity (#PCDATA)>
<!--SequenceData
Data for individual Sequence.
For intentionally skipped sequences see the ST.26 main body document.
-->
<!ELEMENT SequenceData (INSDSeq)>
<!ATTLIST SequenceData
              sequenceIDNumber CDATA #REQUIRED
>
<!--IPOfficeCode
ST.3 code. For example, if the application identification is PCT/IB2013/099999, then IPOfficeCode
value will be "IB" for the International Bureau of WIPO.
-->
<!ELEMENT IPOfficeCode (#PCDATA)>
<!--ApplicationNumberText
The application identification as provided by the office of filing (e.g. PCT/IB2013/099999)
-->
<!ELEMENT ApplicationNumberText (#PCDATA)>
```

```
<!--FilingDate
The date of filing of the patent application for which the sequence listing is submitted in ST.2
format "CCYY-MM-DD", using a 4-digit calendar year, a 2-digit calendar month and a 2-digit day
within the calendar month, e.g., 2015-01-31. For details, please see paragraphs 7 (a) and 11 of WIPO
Standard ST.2.
-->
<!ELEMENT FilingDate (#PCDATA)>
<!--********************************************************************************
* INSD Part
*********************************************************************************

The purpose of the INSD part of this DTD is to define a customized DTD for sequence listings to
support the work of IP offices while facilitating the data exchange with the public repositories.

The INSD part is subset of the INSD DTD v1.5 and as such can only be used to generate an XML
instance as it will not support the complete INSD structure.

This part is based on:

The International Nucleotide Sequence Database (INSD) collaboration.

INSDSeq provides the elements of a sequence as presented in the GenBank/EMBL/DDBJ-style flatfile
formats. Not all elements are used here.
-->
<!--INSDSeq
Sequence data. Changed INSD V1.5 DTD elements, INSDSeq_division and INSDSeq_sequence from optional
to mandatory per business requirements.
-->
<!ELEMENT INSDSeq (INSDSeq_length, INSDSeq_moltype, INSDSeq_division, INSDSeq_other-seqids?,
INSDSeq_feature-table?, INSDSeq_sequence)>
<!--INSDSeq_length
The length of the sequence. INSDSeq_length allows only integer.
-->
<!ELEMENT INSDSeq_length (#PCDATA)>
<!--INSDSeq_moltype
Admissible values: DNA, RNA, AA
-->
<!ELEMENT INSDSeq_moltype (#PCDATA)>
<!--INSDSeq_division
Indication that a sequence is related to a patent application. Must be populated with the value PAT.
-->
<!ELEMENT INSDSeq_division (#PCDATA)>
<!--INSDSeq_other-seqids
In the context of data exchange with database providers, the Patent Offices should populate for each
sequence the element INSDSeq_other-seqids with one INSDSeqid containing a reference to the
corresponding published patent and the sequence identification.
-->
<!ELEMENT INSDSeq_other-seqids (INSDSeqid?)>
<!--INSDSeq_feature-table
Information on the location and roles of various regions within a particular sequence. Whenever the
element INSDSeq_feature-table is used, it must contain at least one feature.
-->
<!ELEMENT INSDSeq_feature-table (INSDFeature+)>
<!--INSDSeq_sequence
The residues of the sequence. The sequence must not contain numbers, punctuation or whitespace
characters.
-->
<!ELEMENT INSDSeq_sequence (#PCDATA)>
<!--INSDSeqid
Intended for the use of Patent Offices in data exchange only.

Format:
pat|{office code}|{publication number}|{document kind code}|{Sequence identification number}
```

```
where office code is the code of the IP office publishing the patent document, publication number is
the publication number of the application or patent, document kind code is the letter codes to
distinguish patent documents as defined in ST.16 and Sequence identification number is the number of
the sequence in that application or patent

Example:
pat|WO|2013999999|A1|123456

This represents the 123456th sequence from WO patent publication No. 2013999999 (A1)
-->
<!ELEMENT INSDSeqid (#PCDATA)>
<!--INSDFeature
Description of one feature.
-->
<!ELEMENT INSDFeature (INSDFeature_key, INSDFeature_location, INSDFeature_quals?)>
<!--INSDFeature_key
A word or abbreviation indicating a feature.
-->
<!ELEMENT INSDFeature_key (#PCDATA)>
<!--INSDFeature_location
Region of the presented sequence which corresponds to the feature.
-->
<!ELEMENT INSDFeature_location (#PCDATA)>
<!--INSDFeature_quals
List of qualifiers containing auxiliary information about a feature.
-->
<!ELEMENT INSDFeature_quals (INSDQualifier+)>
<!--INSDQualifier
Additional information about a feature.
For coding sequences and variants see the ST.26 main body document.
-->
<!--id
Unique identifier for the INSDQualifier to facilitate comparison of versions of a sequence listing
specifically having language-dependent qualifier values in different languages.
-->
<!ELEMENT INSDQualifier (INSDQualifier_name, INSDQualifier_value?, NonEnglishQualifier_value?)>
<!ATTLIST INSDQualifier
                id ID #IMPLIED
>
<!--INSDQualifier_name
Name of the qualifier.
-->
<!ELEMENT INSDQualifier_name (#PCDATA)>
<!--INSDQualifier_value
Value of the qualifier. Where the qualifier is language dependent its value must be in the English
language and typed with the characters set forth in paragraph 40 (b).
-->
<!ELEMENT INSDQualifier_value (#PCDATA)>
<!--NonEnglishQualifier_value
Value of a language-dependent qualifier in a language that is not English and typed with the
characters set forth in paragraph 40 (a). The language is indicated with the attribute
nonEnglishFreeTextLanguageCode.
-->
<!ELEMENT NonEnglishQualifier_value (#PCDATA)>
```

[Annex III follows]

ANNEX III

SEQUENCE LISTING SPECIMEN (XML file)

Version ~~1.4~~ 2.0

*Revision approved by the Committee on WIPO Standards (CWS)
at its ~~eleventh~~ thirteenth session on ~~December 8, 2023~~ November 14, 2025*

The Annex III is available at: https://www.wipo.int/standards/en/xml_material/st26/st26-annex-iii-sequence-listing-specimen.xml

[Annex IV follows]

ANNEX IV

CHARACTER SUBSET FROM THE UNICODE BASIC LATIN CODE TABLE
FOR USE IN AN XML INSTANCE OF A SEQUENCE LISTING

Version ~~1.3~~ 2.0

Revision approved by the Committee on WIPO Standards (CWS)
at its ~~eleventh~~ thirteenth session on ~~December 8, 2023~~ November 14, 2025

The ampersand character (0026) is only permitted as part of a predefined entity. The quotation mark (0022), the apostrophe (0027), the less-than sign (003C), and the greater-than sign (003E) must be represented by their predefined entities. In addition, the ampersand character (0026) must be represented by its predefined entity when used as an ampersand in a value of an attribute or content of an element.

Unicode code point	Character	Name
0020		SPACE
0021	!	EXCLAMATION MARK
0022	“	QUOTATION MARK
0023	#	NUMBER SIGN
0024	$	DOLLAR SIGN
0025	%	PERCENT SIGN
0026	&	AMPERSAND
0027	‘	APOSTROPHE
0028	(	LEFT PARENTHESIS
0029	)	RIGHT PARENTHESIS
002A	*	ASTERISK
002B	+	PLUS SIGN
002C	,	COMMA
002D	-	HYPHEN-MINUS
002E	.	FULL STOP
002F	/	SOLIDUS
0030	0	DIGIT ZERO
0031	1	DIGIT ONE
0032	2	DIGIT TWO
0033	3	DIGIT THREE
0034	4	DIGIT FOUR
0035	5	DIGIT FIVE
0036	6	DIGIT SIX
0037	7	DIGIT SEVEN
0038	8	DIGIT EIGHT
0039	9	DIGIT NINE
003A	:	COLON
003B	;	SEMICOLON
003C	<	LESS-THAN-SIGN
003D	=	EQUALS SIGN
003E	>	GREATER-THAN-SIGN
003F	?	QUESTION MARK
0040	@	COMMERCIAL AT
0041	A	LATIN CAPITAL LETTER A
0042	B	LATIN CAPITAL LETTER B
0043	C	LATIN CAPITAL LETTER C
0044	D	LATIN CAPITAL LETTER D
0045	E	LATIN CAPITAL LETTER E
0046	F	LATIN CAPITAL LETTER F
0047	G	LATIN CAPITAL LETTER G
0048	H	LATIN CAPITAL LETTER H
0049	I	LATIN CAPITAL LETTER I
004A	J	LATIN CAPITAL LETTER J

Unicode code point	Character	Name
004B	K	LATIN CAPITAL LETTER K
004C	L	LATIN CAPITAL LETTER L
004D	M	LATIN CAPITAL LETTER M
004E	N	LATIN CAPITAL LETTER N
004F	O	LATIN CAPITAL LETTER O
0050	P	LATIN CAPITAL LETTER P
0051	Q	LATIN CAPITAL LETTER Q
0052	R	LATIN CAPITAL LETTER R
0053	S	LATIN CAPITAL LETTER S
0054	T	LATIN CAPITAL LETTER T
0055	U	LATIN CAPITAL LETTER U
0056	V	LATIN CAPITAL LETTER V
0057	W	LATIN CAPITAL LETTER W
0058	X	LATIN CAPITAL LETTER X
0059	Y	LATIN CAPITAL LETTER Y
005A	Z	LATIN CAPITAL LETTER Z
005B	[	LEFT SQUARE BRACKET
005C	\	REVERSE SOLIDUS
005D	]	RIGHT SQUARE BRACKET
005E	^	CIRCUMFLEX ACCENT
005F	_	LOW LINE
0060	`	GRAVE ACCENT
0061	a	LATIN SMALL LETTER A
0062	b	LATIN SMALL LETTER B
0063	c	LATIN SMALL LETTER C
0064	d	LATIN SMALL LETTER D
0065	e	LATIN SMALL LETTER E
0066	f	LATIN SMALL LETTER F
0067	g	LATIN SMALL LETTER G
0068	h	LATIN SMALL LETTER H
0069	i	LATIN SMALL LETTER I
006A	j	LATIN SMALL LETTER J
006B	k	LATIN SMALL LETTER K
006C	l	LATIN SMALL LETTER L
006D	m	LATIN SMALL LETTER M
006E	n	LATIN SMALL LETTER N
006F	o	LATIN SMALL LETTER O
0070	p	LATIN SMALL LETTER P
0071	q	LATIN SMALL LETTER Q
0072	r	LATIN SMALL LETTER R
0073	s	LATIN SMALL LETTER S
0074	t	LATIN SMALL LETTER T
0075	u	LATIN SMALL LETTER U
0076	v	LATIN SMALL LETTER V
0077	w	LATIN SMALL LETTER W
0078	x	LATIN SMALL LETTER X
0079	y	LATIN SMALL LETTER Y
007A	z	LATIN SMALL LETTER Z
007B	{	LEFT CURLY BRACKET
007C	|	VERTICAL LINE
007D	}	RIGHT CURLY BRACKET
007E	~	TILDE

[Annex V follows]

ANNEX V

ADDITIONAL DATA EXCHANGE REQUIREMENTS (FOR IPOs ONLY)

Version ~~1.5~~ 2.0

Revision approved by the Committee on WIPO Standards (CWS)
at its ~~eleventh~~ thirteenth session on ~~December 8, 2023~~ November 14, 2025

In the context of data exchange with database providers (INSD members), the IPOs should populate for each sequence the element `INSDSeq_other-seqids` with one `INSDSeqid` containing a reference to the corresponding published patent and the sequence identification number in the following format:

pat|{office code}|{publication number}|{document kind code}|{sequence identification number}

where office code is the code of the IP office publishing the patent document as set forth in ST.3; document kind code is the code for the identification of different kinds of patent documents as set forth in ST.16; publication number is the publication number of the application or patent; and Sequence identification number is the number of the sequence in that application or patent.

Example:

pat|WO|2013999999|A1|123456

Which would be translated into a valid XML instance as:

```
<INSDSeq_other-seqids>
  <INSDSeqid>pat|WO|2013999999|A1|123456</INSDSeqid>
</INSDSeq_other-seqids>
```

Where “123456” is the 123456th sequence from the WO publication no. 2013999999 (A1).

[Annex VI follows]

ANNEX VI

GUIDANCE DOCUMENT WITH ILLUSTRATED EXAMPLES

Version ~~1.7~~ 2.0

Revision approved by the Committee on WIPO Standards (CWS)
at its ~~eleventh~~ thirteenth session on ~~December 8, 2023~~ November 14, 2025

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EXAMPLES.....3.26.vi.9
APPENDIX.....3.26.vi.73

INTRODUCTION

This Standard indicates as one of its purposes, to "allow applicants to draw up a single sequence listing in a patent application acceptable for the purposes of both international and national or regional procedures." The purpose of this Guidance Document is to ensure that all applicants and Intellectual Property Offices (IPOs) understand and agree on the requirements for inclusion and representation of sequence disclosures, such that this purpose is realized.

This guidance document consists of this introduction, an example index, examples of sequence disclosures, and an appendix containing a sequence listing in XML with sequences from the examples. This introduction explains certain concepts and terminology used in the remainder of this document. The examples illustrate the requirements of specific paragraphs of the Standard and each example has been designated with the most relevant paragraph number. Some examples further illustrate other paragraphs and appropriate cross-references are indicated at the end of each example. The index provides page numbers for the examples ~~and any indicated cross-references~~. Each sequence in an example that either must or may be included in a sequence listing has been assigned a sequence identification number (SEQ ID NO) and appears in XML format in the Appendix to this document.

For each example, any explanatory information presented with a sequence is intended to be considered as the entirety of the disclosure concerning that sequence. The given answers take into account only the information explicitly presented in the example.

The guidance provided in this document is directed to the preparation of a sequence listing for provision on the filing date of a patent application. Preparation of a sequence listing for provision subsequent to the filing date of a patent application must take into account whether the information provided could be considered by an IPO to add subject matter to the original disclosure. Therefore, it is possible that the guidance provided in this document may not be applicable to a sequence listing provided subsequent to the filing date of a patent application.

Preparation of a sequence listing

Sequence listing preparation for a patent application requires consideration of the following questions:

1. Does ST.26 paragraph 7 require inclusion of a particular disclosed sequence?

2. If inclusion of a particular disclosed sequence is not required, is inclusion of that sequence permitted by ST.26?

3. If inclusion of a particular disclosed sequence is required or permitted by ST.26, how should that sequence be represented in the sequence listing?

Regarding the first question, ST.26 paragraph 7 (with certain restrictions) requires inclusion of a sequence disclosed in a patent application by enumeration of its residues, where the sequence contains ten or more specifically defined nucleotides or four or more specifically defined amino acids.

Regarding the second question, ST.26 paragraph 8 ~~prohibits~~ permits inclusion of ~~any~~ sequences having fewer than ten specifically defined nucleotides or four specifically defined amino acids.

A clear understanding of "enumeration of its residues" and "specifically defined" is necessary to answer these two questions.

Regarding the third question, this document provides sequence disclosures which exemplify a variety of scenarios together with a complete discussion of the preferred means of representation of each sequence, or where a sequence contains multiple variations - the "most encompassing sequence", in accordance with this Standard. Since it is impossible to address every possible unusual sequence scenario, this guidance document attempts to set forth the reasoning behind the approach to each example and the manner in which ST.26 provisions are applied, such that the same reasoning can be applied to other sequence scenarios not exemplified.

Enumeration of its residues

ST.26 paragraph 3(c) defines "enumeration of its residues" as disclosure of a sequence in a patent application by listing, in order, each residue of the sequence, wherein (i) the residue is represented by a name, abbreviation, symbol, or structure; or (ii) multiple residues are represented by a shorthand formula. A sequence should be disclosed in a patent application by "enumeration of its residues" using conventional symbols, which are the nucleotide symbols set forth in Section 1, Table 1 of ST.26 Annex 1 (i.e., the ~~lower case~~lower-case symbols or their upper-case equivalents[1]) and the amino acid symbols set forth in Section 3, Table 3 of ST.26 Annex 1 (i.e., the ~~upper~~ upper-case symbols or their ~~lower~~ lower-case equivalents[1]) or the three-letter abbreviations set forth in Annex VI, Table B. ~~.~~ Hereinafter, these nucleotide and amino acid symbols are referred to as conventional symbols. Representations of nucleotides and amino acids that are other than those set forth in these tables are hereinafter referred to as "nonconventional".

Where a representation of a residue is disclosed as equivalent to a conventional symbol or abbreviation (e.g., "Z_1" means "A"), or to a specific sequence of conventional symbols (e.g., "Z_1" means "agga"), then the sequence is interpreted as though it were disclosed using the equivalent conventional symbol(s) or abbreviation(s), to determine whether ST.26 paragraph 7 requires inclusion in the sequence listing ~~or whether paragraph 8 prohibits inclusion~~. Where a nonconventional nucleotide symbol is used as an ambiguity symbol (e.g., X1 = inosine or pseudouridine), but is not equivalent to one of the conventional ambiguity symbols in Section 1, Table 1 (i.e., "m", "r", "w", "s", "y", "k", "v", "h", "d", "b", or "n"), then the residue is interpreted as an "n" residue to determine whether ST.26 Paragraph 7 requires inclusion of the sequence in the sequence listing ~~or whether ST.26 Paragraph 8 prohibits inclusion~~. Similarly, where a nonconventional amino acid symbol is used as an ambiguity symbol (e.g., "Z_1" means "A", "G", "S" or "T"), but is not equivalent to one of the conventional ambiguity symbols in Section 3, Table 3 (i.e., B, Z, J, or X), then the residue is interpreted as an "X" residue to determine whether ST.26 paragraph 7 requires inclusion of the sequence in the sequence listing ~~or whether ST.26 paragraph 8 prohibits inclusion~~.

Care should be taken to disclose sequences using conventional symbols; however, where sequences are otherwise disclosed, it may be necessary to consult the disclosure for an explanation to determine the meaning of the nonconventional representation.

Where a conventional symbol is used, the explanation of the sequence in the disclosure must still be consulted to confirm that the symbol is used in a conventional manner. If the symbol is used in a nonconventional manner, this explanation is necessary to determine whether ST.26 paragraph 7 requires inclusion of the sequence in the sequence listing ~~or whether paragraph 8 prohibits inclusion~~.

Specifically defined

ST.26 paragraph 3(k) defines "specifically defined" as any nucleotide other than those represented by the symbol "n" and any amino acid other than those represented by the symbol "X", listed in Annex I, wherein "n" and "X" are used in a conventional manner as described in Section 1, Table 1 (i.e., "a or c or g or t/u; 'unknown' or 'other'") and Section 3, Table 3 (i.e., "A or R or N or D or C or Q or E or G or H or I or L or K or M or F or P or O or S or U or T or W or Y or V; 'unknown' or 'other'"), respectively. The discussion above concerning conventional symbols or nonconventional symbols or abbreviations and their use in a conventional or nonconventional manner will be taken into account to determine whether a nucleotide or an amino acid is "specifically defined".

[1] NOTE: While an application disclosure may represent nucleotides or amino acids with either lower-case or upper-case symbols, for a sequence included in a sequence listing, only lower-case letters must be used for representation of a nucleotide sequence (see ST.26 paragraph 13) and only upper-case letters must be used for representation of an amino acid sequence (see ST.26 paragraph 26).

Most encompassing sequence

Where a sequence that meets the requirements of paragraph 7 is disclosed by enumeration of its residues only once in an application, but is described differently in multiple embodiments, e.g., one embodiment "X" in one or more locations could be any amino acid, but in further embodiments, "X" could be only a limited number of amino acids, ST.26 requires inclusion in a sequence listing of only the single sequence that has been enumerated by its residues. As per paragraphs 15 and 27, where such a sequence contains ~~multiple~~ the "n" or "X" ambiguity symbol~~s~~, "n" ~~or "X" is~~ will be construed ~~to represent~~as any one of the unmodified nucleotide~~s~~ "a", "c", "g", or "t/u" and "X" will be construed as any one of the unmodified L-alpha-~~or~~ amino acid~~s~~ "A", "R", N", "D", "C", "Q", "E", "G", "H", "I", "L", "K", "M", "F", "P", "O", "S", "U", "T", "W", "Y", or "V", respectively, in the absence of further annotation. Consequently, the single sequence required to be included is the most encompassing sequence disclosed. The most encompassing sequence is the single sequence having variant residues that are represented by the most restrictive ambiguity symbols that include the most disclosed embodiments. Likewise, where a sequence is disclosed by enumeration of its residues only once, but the length of the sequence may vary due to copy number variation, the longest embodiment of the sequence is considered the most encompassing sequence. For example, consider a sequence containing a repeated region that can vary from 2 to 5 copies as enumerated. The embodiment with 5 copies of the repeat is the most encompassing sequence and should be included in the sequence listing. However, inclusion of additional specific sequences is strongly encouraged where practical, e.g., those that represent additional embodiments that are a key part of the invention. Inclusion of the additional sequences allows for a more thorough search and provides public notice of the subject matter for which a patent is sought.

Usage of Ambiguity Symbol

Proper Usage of the Ambiguity Symbol "n" in a Sequence Listing

The symbol "n"

a. must not be used to represent anything other than a single nucleotide;

b. will be construed as any one of the following unmodified nucleotides "a", "c", "g", or "t/u" except where it is used with a further description;

c. ~~should~~ must be used together with a further description to represent any of the following nucleotides ~~together with a further description~~:

   i. a natural or non-natural modified nucleotide comprising a modified nucleobase~~, e.g., natural, synthetic, or non-naturally occurring~~, that cannot otherwise be represented by any other symbol in Annex I (see Section 1, Table 1);

   ii. an "unknown" nucleotide, i.e., not determined, not disclosed, or unsure;

   iii. an abasic site; ~~or~~

d. must not be used to represent a modified nucleotide comprising a nucleobase identical to that of a nucleotide listed in Annex I, Section 1, Table 1; and

e. may be used to represent a sequence variant, i.e., alternatives, deletions, insertions, or substitutions, where "n" is the most restrictive ambiguity symbol.

Proper Usage of the Ambiguity Symbol "X" in a Sequence Listing

The symbol "X"

a. must not be used to represent anything other than a single amino acid;

b. will be construed as ~~any~~ one of the unmodified L-alpha-amino acids "A", "R", "N", "D", "C", "Q", "E", "G", "H", "I", "L", "K", "M", "F", "P", "O", "S", "U", "T", "W", "Y", or "V", except where it is used with a further description;

c. ~~should~~ must be used together with a further description to represent any of the following amino acids ~~together with a further description~~:

   i. ~~modified amino acid, e.g.,~~ a natural~~, synthetic,~~ or non-~~naturally~~ natural modified amino acid ~~occurring~~comprising a modified side chain~~,~~ that cannot otherwise be represented by any other symbol in Annex I (see Section 3, Table 3);

ii. an "unknown" amino acid, i.e., not determined, not disclosed, or unsure; or

d. must not be used to represent a modified amino acid with a single carbon-containing side chain identical to the side chain of an L-alpha amino acid listed in Annex I, Section 1, Table 3; and

e. may be used to represent a sequence variant, i.e., alternatives, deletions, insertions, or substitutions, where "X" is the most restrictive ambiguity symbol.

Annotation of Modified Residues

This Standard requires that "modified" residues are annotated per paragraph 17 for nucleotides, and per paragraph 30 for amino acids.

ST.26 paragraph 3(e) defines "modified amino acid" as any amino acid as described in paragraph 3(a) other than the following L-alpha-amino acids: L-alanine, L-arginine, L-asparagine, L-aspartic acid, L-cysteine, L-glutamine, L-glutamic acid, L-glycine, L-histidine, L-isoleucine, L-leucine, L-lysine, L-methionine, L-phenylalanine, L-proline, L-pyrrolysine, L-serine, L-selenocysteine, L-threonine, L-tryptophan, L-tyrosine, or L-valine. Similarly, the Standard defines "modified nucleotide" as any nucleotide as described in paragraph 3(g) other than deoxyadenosine 5'- monophosphate, deoxyguanosine 5'-monophosphate, deoxycytidine 5'-monophosphate, deoxythymidine 5'- monophosphate, adenosine 5'-monophosphate, guanosine 5'-monophosphate, cytidine 5'-monophosphate, or uridine 5'- monophosphate (ST.26, paragraph 3(f)).

Based on the definitions above, modifications to the nucleobases or sugar-phosphate backbone of a nucleic acid and modifications to the amino acid ~~R-groups~~side chains or ~~peptide~~ amide backbone of a peptide result in one or more "modified nucleotides" or "modified amino acids," respectively. Therefore, such nucleotides and amino acids must be annotated. Examples of backbone modifications include phosphorothioate linkages in nucleic acids, nucleotide analogs such as peptide nucleic acids (PNA), glycol nucleic acids (GNAs), N-substituted glycines and D-amino acids~~nucleotide analogs such as peptide nucleic acids (PNAs) and glycol nucleic acids (GNAs), and D-amino acids.~~

Note that modification of a terminal amino acid of a peptide or a terminal nucleotide of a nucleic acid does not necessarily result in a "modified amino acid" or "modified nucleotide". One must look at the terminal modification and determine whether the modification changes the chemical structure of the residue such that the residue falls outside the exceptions set forth within paragraph 3(e) and 3(f). For example, a ~~peptide in which the~~ C terminal residue that is linked to a structure (such as part of a branched sequence – see peptide #2 in example 7(b)-3) via a conventional amide linkage is not considered a "modified residue"~~ and therefore is not required to be annotated~~. Similarly, an ~~peptide in which the~~ N terminal residue that is amide bonded to biotin is not considered a "modified residue"~~ and therefore is not required to be annotated~~. In both scenarios, the structure of the residue involved in the C-terminal or N-terminal linkage is not changed from ~~the~~ that of a conventional amino acids recited in paragraph 3(e) of the Standard. However, it is highly recommended that these linkages are annotated using a "SITE" feature key for amino acids or a "misc_feature" feature key for nucleotides.

In contrast, terminal modifications that change the chemical structure of the residue are considered "modified residues" and must be annotated. For example, the methylation of the C-terminus in Example 3(c)-1 does change the chemical structure of the terminal residue, since the methyl group replaces the hydroxyl normally found at the alpha carboxyl group. Therefore, this methylated lysine must be annotated as a "modified residue".

Note that it will be up to the applicant to evaluate each terminal residue modification within an enumerated sequence and make a determination as to whether or not the structure of the terminal residue is changed. If the modified residue structure is different from the conventional amino acids or nucleotides indicated in paragraph 3(e) and 3(f) of the Standard, then the modification must be annotated.

Finally, it is always recommended that applicants include as much information as reasonable in their sequence listings to represent their disclosures as accurately as possible. Therefore, even if a modification isn't required to be annotated, it should preferably be included.

Note however that annotation of variants of an enumerated, primary sequence must comply with the requirements of ~~in~~ ST.26 paragraphs 93-100. Modifications that are disclosed as variants of an enumerated sequence may not be required to be included in the sequence listing. For the definition of annotation of variants, see ST.26 paragraphs 93-95.

Representation of Modified Residues

ST.26 requires that a modified nucleotide with a nucleobase identical to a nucleobase in a nucleotide listed in Annex I, Section 1, Table 1 be represented in the sequence as by the symbol for the corresponding unmodified nucleotide. Likewise, a modified amino acid with a single carbon-containing side chain that is identical to the side chain in an L-alpha-amino acid listed in Annex I, Section 3, Table 3, must be represented in the sequence asby the symbol for the corresponding unmodified amino acid. ST.26 indicates that All other modified nucleotides and amino acids should be represented in the sequence listing as by the symbol for the corresponding unmodified residue whenever possible (see paragraphs 16 and 29). f Note that For modified residues that do not have a nucleobase identical to a nucleobase of a nucleotide listed in Annex I, Section 1, Table 1 or a side chain identical to the side chain in an L-alpha-amino acid listed in Annex I, Section 3, Table 3, representation by the corresponding unmodified residue is a "should" – a "strongly encouraged approach, but not a requirement" (see paragraph 4(d)). In these cases, it is up to the discretion of the applicant to decide if a modified residue will be represented by the symbol for the corresponding unmodified residue or the variable "n" or "X".thisthbysymbol for the recommendation is a "should" – a "strongly encouraged approach, but not a requirement" (see paragraph 4(d)). It is up to the discretion of the applicant to decide if a modified residue will be represented by the symbol for the corresponding unmodified residue or the variables "n" or "X".

As a general rule of thumb – if a nucleobase or amino acid side chainresidue is modified in a way that does not greatly change the structure by the addition of a moiety, such as methylation or acetylation, and the structure of the unmodified residue is generally unchanged, then representation by the symbol for the unmodified residue is recommended. In general, the addition of a moiety to a nucleobase or side chain, such as by methylation, glycosylation, or acetylation, does not substantially change the structure of the nucleobase or side chain. For exampleAccordingly, a methylated adenineadenosine should preferably be represented by "a" in the sequence listing and not "n". A glycosylated serine should preferably be represented by "S" in the sequence listing and not "X". However, when theif a modified residue nucleobase or amino acid side chain is structurally very different in structure from that of any unmodified residue, then representation by an "n" or an "X" is recommended. For example, norleucine is an isomer of leucine, and its side chain is a linear structure of 4 carbons. Leucine also has a 4-carbon side chain, but it is branched at the second carbon. Therefore, the side chain of norleucine isn't simply the result of a modification added to a leucine, buthas a completely different (although related) structure than the side chain of leucine. Accordingly, it is therefore recommended that nNorleucine be represented by an "X" in a sequence listing, and not "L".

How an applicant chooses to represent a modified nucleotide or amino acid that is not required to be represented by the symbol for the corresponding unmodified residue will determine if the residue is "specifically defined". A nucleotide is "specifically defined" when it is represented by anything other than "n"n", and an amino acid is "specifically defined" when it is represented by anything other than "X"X" (see ST.26, paragraph 3(k)). Therefore, a 2' O-methyl adenosine represented by an "a"a" in the sequence is specifically defined, whereas norleucine represented by an "X"X" in the sequence is not specifically defined.

Table A – Conventional Nucleotide Symbols, and Definitions

Symbol	Definition
a	adenine
c	cytosine
g	guanine
t	thymine in DNA uracil in RNA (t/u)
m	a or c
r	a or g
w	a or t/u
s	c or g
y	c or t/u
k	g or t/u

Symbol	Definition
v	a or c or g; not t/u
h	a or c or t/u; not g
d	a or g or t/u; not c
b	c or g or t/u; not a
n	a or c or g or t/u; “unknown” or “other”

Table B – Conventional Amino Acid Symbols, Three letter Codes, and Definitions

Symbol	3-Letter Code	Definition
A	Ala	Alanine
R	Arg	Arginine
N	Asn	Asparagine
D	Asp	Aspartic Acid (Aspartate)
C	Cys	Cysteine
Q	Gln	Glutamine
E	Glu	Glutamic Acid (Glutamate)
G	Gly	Glycine
H	His	Histidine
I	Ile	Isoleucine
L	Leu	Leucine
K	Lys	Lysine
M	Met	Methionine
F	Phe	Phenylalanine
P	Pro	Proline
O	Pyl	Pyrrolysine
S	Ser	Serine
U	Sec	Selenocysteine
T	Thr	Threonine
W	Trp	Tryptophan
Y	Tyr	Tyrosine
V	Val	Valine
B	Asx	Aspartic Acid or Asparagine
Z	Glx	Glutamine or Glutamic Acid
J	Xle	Leucine or Isoleucine
X	Xaa	A or R or N or D or C or Q or E or G or H or I or L or K or M or F or P or O or S or U or T or W or Y or V, “unknown” or “other”

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EXAMPLES

Paragraph 3(a) – Definition of "amino acid"

Example 3(a)-1: D-amino acids

A patent application describes the following sequence:

Cyclo (D-Ala-D-Glu-Lys-Nle-Gly-D-Met-D-Nle)

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

Paragraph 3(a) of the Standard defines "amino acid" as including "D-amino acids" and amino acids containing modified or synthetic side chains. Based on this definition, the enumerated peptide contains ~~five~~ seven amino acids. The "Lys" in position 3 and the "Gly" in position 5 are specifically defined. Paragraph 29 of the Standard requires representation of a D-amino acid having a single carbon-containing side chain that is identical to the side chain in an L-alpha-amino acid listed in Annex I, Section 3, Table 3 by the symbol of the corresponding unmodified amino acid. Accordingly, the D-Ala in position 1, the D-Glu in position 2, and the D-Met in position 6 must be represented by "A," "E," and "M," respectively, and are also specifically defined ~~that are specifically defined (D-Ala, D-Glu, Lys, Gly, and D-Met)~~. Therefore, minimally, the sequence contains 5 specifically defined amino acid and must be included in a sequence listing as required by ST.26 paragraph 7(b).

Question 3: How should the sequence(s) be represented in the sequence listing?

The Nle in position 4 and the D-Nle in position 7 do not have side chains identical to the side chain in an L-alpha-amino acid listed in Annex I, Section 3, Table 3. Therefore, norleucine and D-norleucine may be represented in the sequence by the symbol "X" or the most appropriate amino acid symbol. ~~Paragraph 29 requires that D-amino acids should be represented in the sequence as the corresponding unmodified L-amino acid. Further, any modified amino acid that cannot be represented by any other symbol in Annex I, Section 3, Table 3, must be represented by the symbol "X".~~

~~In this example, the sequence contains three D-amino acids that can be represented by an unmodified L-amino acid in Annex I, Section 3, Table 3, one L-amino acid (Nle), and one D-amino acid (D-Nle) that must be represented by the symbol "X".~~

Paragraph 25 indicates that when amino acid sequences are circular in configuration and the ring consists solely of amino acid residues linked by ~~peptide~~ amide bonds, applicant must choose the amino acid in residue position number 1. Accordingly, the sequence may be represented as:

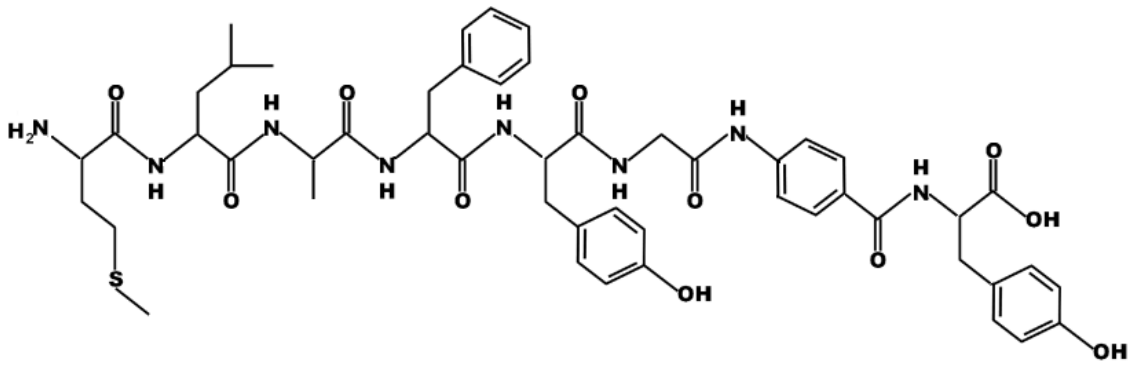
AEKXGMX (SEQ ID NO: 1)

or otherwise, with any other amino acid in the sequence in residue position number 1. A feature key "SITE" and a qualifier "note" must be provided for each D-amino acid with the complete, unabbreviated name of the D-amino acid as the qualifier value, e.g., D-alanine and D-norleucine. Further, a feature key "SITE" and a qualifier "note" must be provided with the abbreviation for L-norleucine as the qualifier value, i.e. "Nle", as set forth in Annex I, Section 4, Table 4. Finally, a feature key "REGION" and a qualifier "note" should be provided to indicate that the peptide is circular.

Relevant ST.26 paragraphs: 3(a), 7(b), 25, 26, 29, 30, and 31

Example 3(a)-2: Organic molecule with an amino group and a carboxyl group

A patent application discloses the peptide sequence Met-Leu-Ala-Phe-Tyr-Gly-(4-aminobenzoic acid)-Tyr having the structure:



Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

Paragraph 7(b) requires inclusion of any unbranched sequence that contains four or more specifically defined amino acids, where the amino acids form a single peptide backbone. Because there are seven specifically defined amino acids within the sequence, ST.26 paragraph 7(b) requires that the sequence be included in a sequence listing.

Question 3: How should the sequence(s) be represented in the sequence listing?

The 4-aminobenzoic acid present in the 7th position is construed as an amino acid within the meaning of paragraph 3(a). Paragraph 3(a) indicates that an amino acid is "an organic molecule containing an amino group and a carboxyl group." The 4-aminobenzoic acid in position 7 is an organic molecule containing an amino group and a carboxyl group; therefore, it meets the definition of an amino acid. Since the 4-aminobenzoic acid is joined to adjacent amino acids by amide bonds as part of a single peptide backbone, the disclosed peptide of eight residues must be represented in the sequence listing as a single sequence.

4-aminobenzoic acid is a "modified amino acid" that does not have a side chain that is identical to the side chain of any of the L-alpha-amino acids listed in Annex I, Section 3, Table 3. According to ST.26 paragraph 29, a modified amino acid should be represented in the sequence as the corresponding unmodified amino acid whenever possible. The symbol "X" should only be used to represent a modified amino acid when none of the other symbols in Annex I, Section 3, Table 3 is suitable. Accordingly, 4-aminobenzoic acid should be represented in the sequence by the symbol "X," and the sequence should be represented as:

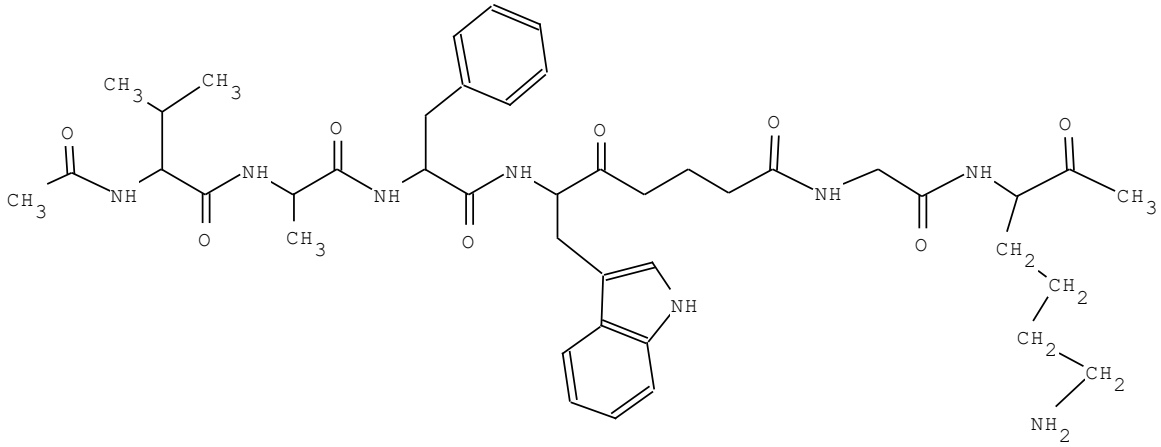
MLAFYGXY (SEQ ID NO: 103)

The 4-aminobenzoic acid in position 7 must be described according to paragraph 29 using the feature key "SITE" and the mandatory qualifier "note" with a value that is the complete unabbreviated name of the modified amino acid, e.g., "4-aminobenzoic acid."

Relevant ST.26 paragraph(s): 3(a), 3(e), 7(b), 29, 30, 31

Paragraph 3(c) – Definition of "enumeration of its residues"

Example 3(c)-1: Enumeration of amino acids by chemical structure



Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

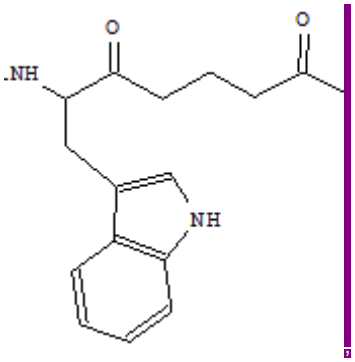
The enumerated peptide, illustrated as a structure, contains at least four specifically defined amino acids. Therefore, the sequence must be included in a sequence listing.

Question 3: How should the sequence(s) be represented in the sequence listing?

The sequence ~~may~~ should be represented as:

~~VAFXGK~~ VAFWGK (SEQ ID NO: 2)

~~wherein "X" represents an "other" modified amino acid~~The side chain of the fourth residue is identical to a side chain in an L-alpha-amino acid listed in Annex I, Section 3, Table 3:



According to paragraph 29, it must be represented in the sequence using the symbol of the corresponding unmodified amino acid, which is tryptophan (symbol W). As prescribed by paragraph 30, this modified residue must further be described using the~~which requires a~~ feature key "SITE" together with the qualifier "note". The qualifier "note" provides the complete, unabbreviated name of the modified tryptophan in position 4 of the enumerated peptide, e.g., "6-amino-7-(1H-indol-3-yl)-5-oxoheptanoic acid".

The methylation of the C terminus of the peptide changes the chemical structure of the terminal lysine since the -OH on the terminal end is replaced by -CH3. Due to this structural change, the lysine within the sequence is considered a "modified amin~~a~~o acid." Accordingly, a feature key "SITE" and qualifier "note" are required to indicate the methylation of the C-terminus. However, valine at the N terminus, ~~however,~~ is not considered a "modified amino acid" since the addition of the acetyl group to the valine involves a conventional peptide linkage. The acetylation does not alter the structure of the valine. Accordingly, an additional feature key "SITE" and qualifier "note" should be included to indicate the acetylation of the N-terminus.

~~Alternatively, the sequence may be represented as:~~

~~VAFW (SEQ ID NO: 3)~~

~~A feature key "SITE" and qualifier "note" are required to indicate modification of tryptophan in position 4 of the enumerated peptide with the value: "C-terminus linked via a glutaraldehyde bridge to dipeptide GK". Further, an additional feature key "SITE" at location 1 and qualifier "note" should be included to indicate the acetylation of the N-terminus.~~

Relevant ST.26 paragraph(s): **3(a), 3(c)**, 7(b), 29, 30, and 31

Example 3(c)-2: Shorthand formula for an amino acid sequence

$(G_4z)_n$

Where G= Glycine, z = any amino acid and variable n can be any whole integer.

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The disclosure indicates that "n" can be "any whole integer"; therefore, the most encompassing embodiment of "$(G_4z)_n$" is indeterminate. Since "n" is indeterminate, the peptide of the formula cannot be expanded to a definite length, and therefore, the unexpanded formula must be considered.

The enumerated peptide in the unexpanded formula ("n" = 1) provides four specifically defined amino acids, each of which is Gly, and the symbol "z". Conventionally "Z" is the symbol for "glutamine or glutamic acid"; however, the example defines "z" as "any amino acid". Under ST.26, an amino acid that is not specifically defined is represented by "X". Based on this analysis, the enumerated peptide, i.e. GGGGX, contains four glycine residues that are enumerated and specifically defined. Thus, ST.26 paragraph 7(b) requires inclusion of the sequence in a sequence listing.

Question 3: How should the sequence(s) be represented in the sequence listing?

The sequence uses a nonconventional symbol "z", the definition of which must be determined from the disclosure (see Introduction to this document). Since "z" is defined as any amino acid, the conventional symbol used to represent this amino acid is "X." Therefore, the sequence must be represented as a single sequence:

GGGGX (SEQ ID NO: 4)

and should be annotated with the feature key REGION, feature location ">5" (corresponds to >5), with a note qualifier with the value "The entire sequence of amino acids 1-5 can be repeated one or more times."

According to paragraph 27, "X" will be construed as any one of the unmodified L-alpha amino acids: "A", "R", "N", "D", "C", "Q", "E", "G", "H", "I", "L", "K", "M", "F", "P", "O", "S", "U", "T", "W", "Y", or "V", except where it is used with a further description in the feature table. ~~Since i~~In this example "X" represents "any amino acid", which is broader in scope than the default value of "X" set forth in paragraph 27, since "any amino acid" encompasses modified or other amino acids. Therefore, the "X" in this sequence ~~it~~must be annotated with the feature key VARIANT and a note qualifier with the value, "X can be any amino acid".

~~Where practicable, each "X" should be annotated individually. However, a region of contiguous "X" residues, or a multitude of "X" residues dispersed throughout the sequence, may be jointly described with the feature key VARIANT using the syntax "x..y" as the location descriptor, where x and y are the positions of the first and last "X" residues, and a note qualifier with the value, "X can be any amino acid".~~

CAUTION: The preferred representation of the sequence indicated above is directed to the provision of a sequence listing on the filing date of a patent application. The same representation may not be applicable to a sequence listing provided subsequent to the filing date of a patent application, since consideration must be given to whether the information provided could be considered by an IPO to add subject matter to the original disclosure.

Relevant ST.26 paragraph(s): 3(c), 7(b) and 27.

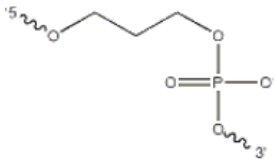
Paragraph 3(g) – Definition of "nucleotide"

Example 3(g)-1: Nucleotide sequence interrupted by a C3 spacer

A patent application describes the following sequence:

atgcatgcatgcncggcatgcatgc

where n = a C3 spacer with the following structure:



Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The enumerated sequence contains two segments of specifically defined nucleotides separated by a C3 spacer.

The C3 spacer is not a nucleotide according to paragraph 3(g); the conventional symbol "n" is being used in a nonconventional manner (see Introduction to this document). Consequently, each segment is a separate nucleotide sequence. Since each segment contains more than 10 specifically defined nucleotides, both must be included in a sequence listing.

Question 3: How should the sequence(s) be represented in the sequence listing?

Each segment must be included in a sequence listing as a separate sequence, each with their own sequence identification number:

atgcatgcatgc (SEQ ID NO: 5)

cggcatgcatgc (SEQ ID NO: 6)

The cytosine in each segment that is attached to the C3 spacer should be further described in a feature table using the feature key "misc_feature" and the qualifier "note". The "note" qualifier value, which is "free text", should indicate the presence of the spacer, which is joined to another nucleic acid and identify the spacer by either its complete unabbreviated chemical name, or by its common name, e.g., C3 spacer.

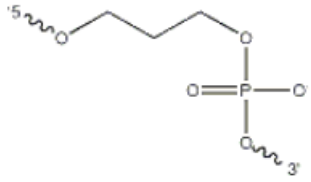
Relevant ST.26 paragraphs: 3(g), 7(a), and 15

Example 3(g)-2: Nucleotide sequence with residue alternatives, including a C3 spacer

A patent application describes the following sequence:

atgcatgcatgcncggcatgcatgc

where n = c, a, g, or a C3 spacer with the following structure:



Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

There are 24 specifically defined residues in the enumerated sequence interrupted by the variable "n." The explanation of the sequence in the disclosure must be consulted to determine if the "n" is used in a conventional or nonconventional manner (see Introduction to this document).

The disclosure indicates that n = c, a, g, or a C3 spacer. The "n" is a conventional symbol used in a nonconventional manner, since it is described as including a C3 spacer, which does not meet the definition of a nucleotide. The symbol "n" is also described as including "c", "a", or "g"; therefore, ST.26 requires inclusion of the 25 nucleotide sequence in a sequence listing. Since two segments separated by the C3 spacer are distinct sequences from the 25 nucleotide sequence, the two 12 nucleotide sequences may also be included.

Question 3: How should the sequence(s) be represented in the sequence listing?

The example indicates that "n = c, a, g, or a C3 spacer". As discussed above, a C3 spacer is not a nucleotide. According to paragraph 15, the symbol "n" must not be used to represent anything other than a nucleotide; therefore, the symbol "n" cannot represent a C3 spacer in a sequence listing.

Paragraph 15 also states that where an ambiguity symbol is appropriate, the most restrictive symbol should be used. The symbol "v" represents "a or c or g" according to Annex I, Section 1, Table 1, which is more restrictive than "n".

Where variable "n" in the example is c, a, or g, the single sequence enumerated by its residues that includes the most disclosed embodiments, and is therefore, the most encompassing sequence (see introduction to this document) that must be included in a sequence listing is:

atgcatgcatgcvcggcatgcatgc (SEQ ID NO: 7)

Inclusion of any additional sequences essential to the disclosure or claims of the invention is strongly encouraged, as discussed in the introduction to this document.

Where variable "n" in the example is a C3 spacer, the sequence can be considered two separate segments of specifically defined nucleotides on either side of the variable "n", i.e. atgcatgcatgc (SEQ ID NO: 8); and cggcatgcatgc (SEQ ID NO: 9). If essential to the disclosure or claims, these two sequences should also be included in the sequence listing, each with their own sequence identification number.

The cytosine in each segment that is attached to the C3 spacer should be further described in a feature table using the feature key "misc_feature" and the qualifier "note". The "note" qualifier value, which is "free text", should indicate the presence of the spacer, which is joined to another nucleic acid and identify the spacer by either its complete unabbreviated chemical name, or by its common name, e.g., C3 spacer.

CAUTION: The preferred representation of the sequence indicated above is directed to the provision of a sequence listing on the filing date of a patent application. The same representation may not be applicable to a sequence listing provided subsequent to the filing date of a patent application, since consideration must be given to whether the information provided could be considered by an IPO to add subject matter to the original disclosure.

Relevant ST.26 paragraphs: 3(g), 7(a), and 15

Example 3(g)-3: Abasic site

A patent application describes the following sequence:

gagcattgac-AP-taaggct

Wherein AP is an abasic site

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The specifically defined residues of the enumerated sequence are interrupted by an abasic site. The 5' side of the abasic site contains 10 nucleotides and the 3' side of the abasic site contains 7 nucleotides. Paragraph 3(g)(ii)(2) defines an abasic site as a "nucleotide" when it is part of a nucleotide sequence. Consequently, the abasic site in this example is considered a "nucleotide" for the purposes of determining if and how the sequence is required to be included in a sequence listing. Accordingly, the residues on each side of the abasic site are part of a single enumerated sequence containing 18 nucleotides total, 17 of which are specifically defined. Therefore, the sequence must be included as a single sequence in a sequence listing as required by ST.26 paragraph 7(a).

Question 3: How should the sequence(s) be represented in the sequence listing?

The sequence must be included in a sequence listing as:

gagcattgacntaaggct (SEQ ID NO: 10)

The abasic site must be represented by an "n" and must be further described in a feature table. The preferred means of annotation is the feature key "modified_base" and the mandatory qualifier "mod_base" with the value "OTHER". A "note" qualifier must be included that describes the modified base as an abasic site.

Relevant ST.26 paragraphs: 3(g), 7(a), and 17

Example 3(g)-4: Nucleic Acid Analogues

A patent application discloses the following glycol nucleic acid (GNA) sequence:

PO_4-tagttcattgactaaggctccccattgact-OH

Wherein the left end of the sequence mimics the 5' end of a DNA sequence.

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The individual residues that comprise a GNA sequence are considered modified nucleotides according to ST.26 paragraphs 3(f) and 3(g)(i)(2). ST.26 paragraph 16 requires that a modified nucleotide that has a nucleobase identical to a nucleobase in an unmodified nucleotide listed in Annex I, Section 1, Table 1 be represented in the sequence as the corresponding unmodified nucleotide. Therefore, each residue in the sequence must be represented by the corresponding unmodified residue symbol, making each residue specifically defined. Accordingly, the sequence has more than ten enumerated and "specifically defined" nucleotides and is required to be included in a sequence listing.

Question 3: How should the sequence(s) be represented in the sequence listing?

GNA sequences do not have a 5'-end and a 3'-end, but rather, a 3'-end and a 2'-end. The 3'-end, which is routinely depicted as having a terminal phosphate group, corresponds to the 5'-end of DNA or RNA. (Note that other nucleic acid analogues may correspond differently to the 5'-end and 3'-end of DNA and RNA.) According to paragraph 11, it must be included in a sequence listing "in the direction from left to right that mimics the 5'-end to 3'-end direction." Therefore, it must be included in a sequence listing as:

tagttcattgactaaggctccccattgact (SEQ ID NO: 11)

Each nucleotide of the sequence must be described in a feature table using the feature key "modified_base" and the mandatory qualifier "mod_base" with the abbreviation "OTHER". A "note" qualifier must be included with the complete unabbreviated name of the modified nucleotides. According to ST.26 paragraph 18, as all of the modified nucleotides in the sequence share the same backbone moiety, the region may be jointly described in a feature table with "1..30" as the location descriptor, the feature key "modified_base", the mandatory qualifier "mod_base" with the abbreviation "OTHER" and a "note" qualifier with a value that is the most restrictive unabbreviated chemical name that encompasses all of the modified nucleotides in the range, such as "glycol nucleic acids" or "2,3-dihydroxypropyl nucleosides". ~~A single INSDFeature element can be used to describe the entire sequence as a GNA where the INSDFeature_location has the range "1..30".~~

Relevant ST.26 paragraphs: 3(f), **3(g)**, 7(a), 11, 16, 17, 18, 22, 65, and 66

Paragraph 3(k) – Definition of "specifically defined"

Example 3(k)-1: Nucleotide ambiguity symbols

5' NNG KNG KNG K 3'

N and K are IUPAC-IUB ambiguity codes

Question 1: Does ST.26 require inclusion of the sequence(s)?

NO

IUPAC-IUB ambiguity codes correspond to the list of nucleotide symbols defined in Annex I, Section 1, Table 1. According to paragraph 3(k), a specifically defined nucleotide is any nucleotide other than those represented by the symbol "n" listed in Annex I. Therefore, "K" and "G" are specifically defined nucleotides and "N" is not a specifically defined nucleotide.

The enumerated sequence does not have ten or more specifically defined nucleotides and therefore is not required by ST.26 paragraph 7(a) to be included in a sequence listing.

Question 2: Does ST.26 permit inclusion of the sequence(s)?

~~NO~~**YES**

According to paragraph 8, "A sequence listing ~~must not~~may include ~~any~~ sequences having fewer than ten specifically defined nucleotides…." ~~The enumerated sequence does not have ten or more specifically defined nucleotides; therefore, it must not be included in a sequence listing.~~

Question 3: How should the sequence(s) be represented in the sequence listing?

If included, the sequence should be represented in the sequence listing as:

nngkngkngk (SEQ ID NO: 104)

Note that the default value of "n" specified in paragraph 15 corresponds to the IUPAC-IUB ambiguity code for "n". Therefore, there is no need to annotate each "n" residue as a variant.

Relevant ST.26 paragraphs: 3(k), 7(a), 8, and 13

Example 3(k)-2: Ambiguity symbol "n" used in both a conventional and nonconventional manner

An application discloses the artificial sequence: 5'-AATGCCGGAN-3'. The disclosure further states:

(i) in one embodiment, N is any nucleotide;

(ii) in one embodiment, N is optional but is preferably G;

(iii) in one embodiment, N is K;

(iv) in one embodiment, N is C.

Question 1: Does ST.26 require inclusion of the sequence(s)?

NO

The enumerated sequence contains 9 specifically defined nucleotides and an "N." The explanation of the sequence in the disclosure must be consulted to determine if the symbol "N" is used in a conventional manner (see Introduction to this document).

Consideration of disclosed embodiments (i) through (iv) of the enumerated sequence reveals that the most encompassing embodiment of "N" is "any nucleotide". In the most encompassing embodiment, "N" in the enumerated sequence is used in a conventional manner.

In certain embodiments "N" is described as a specifically defined residues (i.e., "N is C" in part (iv)). However, only the most encompassing embodiment (i.e., "N is any nucleotide") is considered when determining if a sequence must be included in a sequence listing. Thus, the enumerated sequence that must be evaluated is 5'-AATGCCGGAN-3'.

Based on this analysis, the enumerated sequence, i.e. AATGCCGGAN, does not contain ten specifically defined nucleotides. Therefore, ST.26 paragraph 7(a) does not require inclusion of the sequence in a sequence listing, despite the fact that "n" is also defined as specific nucleotides in some embodiments.

Question 2: Does ST.26 permit inclusion of the sequence(s)?

~~NO~~**YES**

The sequence "AATGCCGGAN" ~~must not~~may be included in a sequence listing.

~~However~~Alternatively or in addition, an ~~described~~ alternative sequence may be included ~~with if~~ in a sequence listing if the "N" is ~~being~~ replaced ~~with~~ by a specifically defined nucleotide.

Question 3: How should the sequence(s) be represented in the sequence listing?

If included, the sequence having fewer than ten specifically defined nucleotides should be represented ~~included~~ in the sequence listing as:

aatgccggan (SEQ ID NO: 105)

According to paragraph 15, "n" will be construed as any one of unmodified "a", "c", "g" or "t/u", except where it is used with a further description in the feature table. ~~Since~~

In this example, "n" represents ~~here~~ "any nucleotide", ~~it must be annotated~~which is broader in scope than the default definition of "n" given in paragraph 15, since "any nucleotide" encompasses modified or other nucleotides. Therefore, the "n" must be annotated using the feature key "misc_difference" and a qualifier "note" that describes the "n" as "any nucleotide." The "note" qualifier may also refer to the preferred embodiments: "n can be any nucleotide, preferably g, k or c".

~~In addition or as an alternative to this most encompassing sequence,~~ The inclusion ~~Inclusion~~ of additional sequences which represent embodiments that are a key part of the invention is **strongly** encouraged. Inclusion of these sequences allows for a more thorough search and provides public notice of the subject matter for which a patent is sought.

For the above example, it is highly recommended that the following three additional sequences are included in the sequence listing, each with their own sequence identification number:

aatgccggag (SEQ ID NO: 12)

aatgccggak (SEQ ID NO: 13)

aatgccggac (SEQ ID NO: 14)

If ~~less than all~~ any of the three ~~of the~~ above sequences are included in a sequence listing, the nucleotide that replaces the "n" should be annotated ~~to describe the alternatives. For example, if only SEQ ID NO: 12 above is included in the sequence listing, the~~using the feature key "misc_difference" ~~with feature location "10" should be~~

~~used together with two "replace" qualifiers where the value for one would be "k" and the second would be "c"~~with a mandatory qualifier "note" or "replace" to describe the possible alternatives.

CAUTION: The preferred representation of the sequences indicated above as SEQ ID NOes: 12-14 ~~is~~ are directed to the provision of a sequence listing on the filing date of a patent application. The same representation may not be applicable to a sequence listing provided subsequent to the filing date of a patent application, since consideration must be given to whether the information provided could be considered by an IPO to add subject matter to the original disclosure.

Relevant ST.26 paragraphs: 3(k), 7(a), 8, ~~and~~ 13, and ~~16~~15

Example 3(k)-3: Ambiguity symbol "n" used in a nonconventional manner

An application discloses the sequence: 5'-aatgttggan-3'

Wherein n is c

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

According to paragraph 3(k), a "specifically defined" nucleotide is any nucleotide other than those represented by the symbol "n" listed in Annex I, Section 1, Table 1.

In this example "n" is used in a nonconventional manner to represent only "c". The disclosure does not indicate that "n" is used in the conventional manner to represent "any nucleotide". Therefore, the sequence must be interpreted as if the equivalent conventional symbol, i.e. "c", had been used in the sequence (see Introduction to this document). Accordingly, the enumerated sequence that must be considered is:

5'-aatgttggac-3'

This sequence has ten specifically defined nucleotides and is required by ST.26 paragraph 7(a) to be included in a sequence listing.

Question 3: How should the sequence(s) be represented in the sequence listing?

The sequence must be included in a sequence listing as: aatgttggac (SEQ ID NO: 15)

Relevant ST.26 paragraphs: 3(k) and 7(a)

Example 3(k)-4: Ambiguity symbols other than "n" are "specifically defined"

A patent application describes the following sequence:

5' NNG KNG KNG KAG VCR 3'

wherein N, K, V, and R are IUPAC-IUB ambiguity codes

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

IUPAC-IUB ambiguity codes correspond to the list of nucleotide symbols defined in Annex I, Section 1, Table 1. According to paragraph 3(k), a "specifically defined" nucleotide is any nucleotide other than those represented by the symbol "n" listed in Annex I, Section 1, Table 1. Therefore, "K", "V", and "R" are "specifically defined" nucleotides.

The sequence has eleven enumerated and "specifically defined" nucleotides and is required by ST.26 paragraph 7(a) to be included in a sequence listing.

Question 3: How should the sequence(s) be represented in the sequence listing?

The sequence must be included in a sequence listing as:

nngkngkngkagvcr (SEQ ID NO: 16)

Relevant ST.26 paragraphs: 3(k), 7(a) and 15

Example 3(k)-5: Ambiguity abbreviation "Xaa" used in a nonconventional manner

A patent application describes the following sequence:

Xaa-Tyr-Glu-Xaa-Xaa-Xaa-Leu

Wherein Xaa in position 1 is any amino acid, Xaa in position 4 is Lys, Xaa in position 5 is Gly and Xaa in position 6 is Leucine or Isoleucine.

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The enumerated peptide in the formula provides three specifically defined amino acids in positions 2, 3 and 7. The first amino acid is represented by a conventional abbreviation, i.e., Xaa, representing any amino acid. However, the 4th, 5th and 6th amino acids are represented by a conventional abbreviation used in a nonconventional manner (see Introduction to this document). Therefore, the explanation of the sequence in the disclosure is consulted to determine the definition of "Xaa" in these positions. Since "Xaa" in positions 4-6 are indicated as a specific amino acid, the sequence must be interpreted as if the equivalent conventional abbreviations had been used in the sequence, i.e. Lys, Gly, and (Leu or Ile). Consequently, the sequence contains four or more specifically defined amino acids and must be included in a sequence listing as required by ST.26 paragraph 7(b).

Question 3: How should the sequence(s) be represented in the sequence listing?

The sequence uses a conventional abbreviation "Xaa" in a nonconventional manner. Therefore, the explanation of the sequence in the disclosure must be consulted to determine the definition of "Xaa" in positions 4, 5 and 6. The explanation defines "Xaa" as a lysine in position 4, a glycine in position 5 and a leucine or isoleucine in position 6. The conventional symbols for these amino acids are K, G, and J respectively. Therefore, the sequence should be represented as in the sequence listing as:

XYEKGJL (SEQ ID NO: 17)

According to paragraph 27, "X" will be construed as any one of the following unmodified L-alpha amino acids: "A", "R", "N", "D", "C", "Q", "E", "G", "H", "I", "L", "K", "M", "F", "P", "O", "S", "U", "T", "W", "Y", or "V", except where it is used with a further description in the feature table. Since "X" at position 1 of SEQ ID NO: 17 represents "any amino acid", which is broader in scope than the default value of "X" given in paragraph 27, since "any amino acid" encompasses modified or other amino acids. Therefore, the "X" in this sequence it must be annotated with the feature key VARIANT and a note qualifier with the value, "X can be any amino acid".

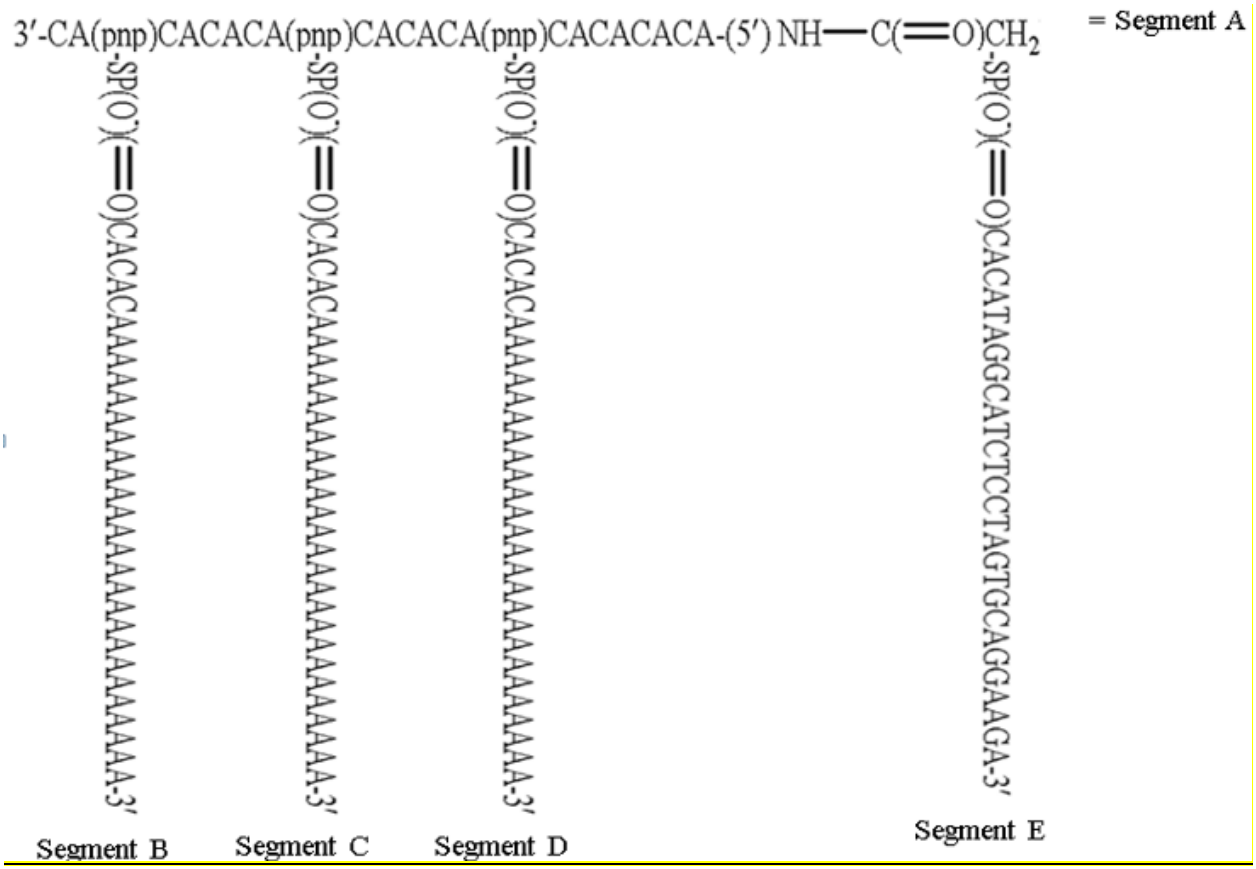
~~Where practicable, each "X" should be annotated individually. However, a region of contiguous "X" residues, or a multitude of "X" residues dispersed throughout the sequence, may be jointly described with the feature key VARIANT using the syntax "x..y" as the location descriptor, where x and y are the positions of the first and last "X" residues, and a note qualifier with the value, "X can be any amino acid".~~

Relevant ST.26 paragraphs: 3(k), 7(b), 26, and 27

Paragraph 7(a) – Nucleotide sequences required in a sequence listing

Example 7(a)-1: Branched nucleotide sequence

The description discloses the following branched nucleotide sequence:



wherein "pnp" is a linkage or monomer containing ~~an~~ a bromoacetylamino functionality;

3’-CA(pnp)CACACA(pnp)CACACA(pnp)CACACACA-(5’)NH—C(=O)CH_2 ~~3'~~ is segment A;

SP(O^-)(=O)CACACAAAAAAAAAAAAAAAAAAAA 3’ is segments B, C, and D; and

SP(O^-)(=O)CACATAGGCATCTCCTAGTGCAGGAAGA 3’ is segment E.

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES – the four vertical segments B-E must be included in a sequence listing

NO – the horizontal segment A must not be included in a sequence listing as a single sequence

The above figure is an example of a “comb-type” branched nucleic acid sequence containing five linear segments: the horizontal segment A and the four vertical segments B-E.

According to paragraph 7(a), the linear regions of branched nucleotide sequences containing ten or more specifically defined nucleotides, wherein adjacent nucleotides are joined 3’ to 5’, must be included in a sequence listing.

The four vertical segments B-E each contain more than ten specifically defined nucleotides, wherein adjacent nucleotides are joined 3’ to 5’, and therefore each is required to be included in a sequence listing.

In horizontal segment A, the linear regions of the nucleotide sequence are linked by the non-nucleotide moiety "pnp" and each of these linked linear regions contains fewer than ten specifically defined nucleotides. Therefore, since no region of segment A contains ten or more specifically defined nucleotides wherein adjacent nucleotides are joined 3' to 5', they are not required by ST.26 paragraph 7(a) to be included in a sequence listing.

Question 2: Does ST.26 permit inclusion of the sequence(s)?

~~NO~~**YES**

According to paragraph 8, "A sequence listing ~~must not~~may include ~~any~~ sequences having fewer than ten specifically defined nucleotides…."

Segment A contains four linear regions of nucleotide sequence separated by the non-nucleotide moiety "pnp". Consequently, segment A cannot be included in a sequence listing as a single sequence, and must be considered four separate sequences. Each of the four separate sequences may be included in a sequence listing with their own SEQ ID number.

~~No region of Segment A contains ten or more specifically defined nucleotides wherein adjacent nucleotides are joined 3' to 5'; therefore, it must not be included in a sequence listing as a separate sequence with its own sequence identification number.~~

~~However, segments B, C, D, and E may be annotated to indicate that they are linked to segment A.~~

Question 3: How should the sequence(s) be represented in the sequence listing?

Segments B, C, and D are identical and must be included in a sequence listing as a single sequence:

cacacaaaaaaaaaaaaaaaaaaaaaaaa (SEQ ID NO: 18)

The first "c" in the sequence should be further described using the feature key "misc_feature" and the qualifier "note" with the value e.g., "This sequence is one of four branches of a branched polynucleotide".

Segment E must be included in a sequence listing as a single sequence:

cacataggcatctcctagtgcaggaaga (SEQ ID NO: 19)

The first "c" in the sequence should be further described using the feature key "misc_feature" and the qualifier "note" with the value e.g., "This sequence is one of four branches of a branched polynucleotide."

The four linear sequences present in segment A may be represented in the sequence listing from 5' to 3' as follows:

acacacac (SEQ ID NO: 106)

acacac (SEQ ID NO: 107)

ac (SEQ ID NO: 108)

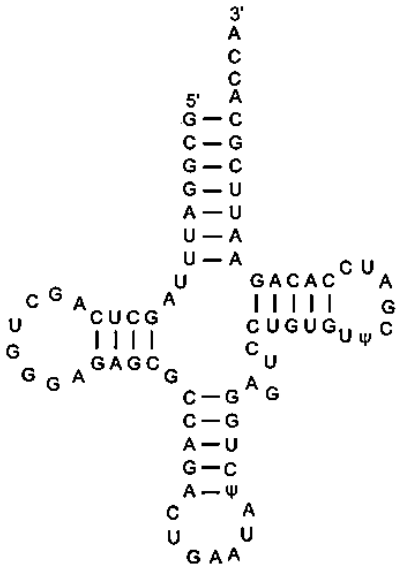
Note that the two internal segments of sequences in Segment A are identical; therefore, one SEQ ID number is sufficient for both.

Each segment should be annotated using the feature key "misc_feature" and the qualifier "note" to indicate that they are modified at the 5' end and/or the 3' end by "pnp" and connected together as part of a larger branched structure.

Relevant ST.26 paragraph(s): 7(a), 8, 11, 13, and 17

Example 7(a)-2: Linear nucleotide sequence having a secondary structure

A patent application describes the following sequence**:**



Wherein Ψ is pseudouridine.

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The nucleotide sequence contains seventy-three enumerated and specifically defined nucleotides. Thus, the example has ten or more “specifically defined” nucleotides, and as required by ST.26 paragraph (7)(a), must be included in a sequence listing.

Question 3: How should the sequence(s) be represented in the sequence listing?

Consultation of the disclosure indicates that “Ψ” is equivalent to pseudouridine. The only conventional symbol that can be used to represent pseudouridine is “n”; therefore, the “Ψ” is a nonconventional symbol used to represent the conventional symbol “n” (see Introduction to this document). Accordingly, the sequence must be interpreted to have two “n” symbols in place of the two “Ψ” symbols.

The symbol “u” must not be used to represent uracil in an RNA molecule in the sequence listing. According to paragraph 14, the symbol “t” will be construed as uracil in RNA. The sequence must be included as:

gcggatttagctcagctgggagagcgccagactgaatanctggagtcctgtgtncgatccacagaattcgcacca (SEQ ID NO: 20)

The value of the mandatory “mol_type” qualifier of the mandatory “source” feature key is “tRNA”. Additional information may be provided with feature key “tRNA” and any appropriate qualifier(s).

The “n” residues must be further described in a feature table using the feature key “modified_base” and the mandatory qualifier “mod_base” with the abbreviation “p” for pseudouridine as the qualifier value (see Annex 1, Table 2).

Relevant ST.26 paragraph(s): 7(a), 11, 13, 14, 17, 62, 84 and Annex I, sections 2 and 5, feature key 5.43

Example 7(a)-3: Nucleotide ambiguity symbols used in a nonconventional manner

A patent application describes the following sequence:

5' GATC-MDR-MDR-MDR-MDR-GTAC 3'

The explanation of the sequence in the disclosure further indicates: "A "DR Element" consists of the sequence 5' ATCAGCCAT 3'. A mutant DR Element, or MDR, is a DR element wherein the middle 5 nucleotides, CAGCC, are mutated to TTTTT."

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The enumerated sequence uses the symbol "MDR". Where it is unclear if a symbol used in a sequence is intended to be a conventional symbol, i.e., a symbol set forth in Annex 1, Section 3, Table 3, or a nonconventional symbol, the explanation of the sequence in the disclosure must be consulted to make a determination (see Introduction to this document). According to Table 3, "MDR" could be interpreted as three conventional symbols (m = a or c, d = a or g or t/u, r = g or a) or as an abbreviation that is short-hand notation for some other structure.

Consultation of the disclosure indicates that an MDR element is equivalent to 5' ATTTTTTAT 3'. The letters "MDR" are considered conventional symbols used in a nonconventional manner; therefore, the sequence must be interpreted as though it were disclosed using the equivalent conventional symbols. Accordingly, the enumerated sequence that is considered for inclusion in a sequence listing is:

5' GATC ATTTTTTAT ATTTTTTAT ATTTTTTAT ATTTTTTAT GTAC 3'

The enumerated sequence has 44 specifically defined nucleotides and is required by ST.26 paragraph 7(a) to be included in a sequence listing.

Question 3: How should the sequence(s) be represented in the sequence listing?

The sequence must be included in a sequence listing as:

gatcatttttatatttttatatttttatatttttatgtac (SEQ ID NO: 21)

Relevant ST.26 paragraphs: 7(a) and 13

Example 7(a)-4: Nucleotide ambiguity symbols used in a nonconventional manner

A patent application describes the following sequence:

5' ATTC-N-N-N-N-GTAC 3'

The explanation of the sequence in the disclosure further indicates that "N" consists of the sequence 5' ATACGCACT 3'.

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The enumerated sequence uses the symbol "N". The explanation of the sequence in the disclosure must be consulted to determine if the "N" is used in a conventional or nonconventional manner (see Introduction to this document).

Consultation of the disclosure indicates that "N" is equivalent to 5' ATACGCACT 3'. Thus, the "N" is a conventional symbol used in a nonconventional manner. Accordingly, the sequence must be interpreted as though it were disclosed using the equivalent conventional symbols:

5' ATTC-ATACGCACT-ATACGCACT-ATACGCACT-ATACGCACT-GTAC 3'

The enumerated sequence has 44 specifically defined nucleotides and is required by ST.26 paragraph 7(a) to be included in a sequence listing.

Question 3: How should the sequence(s) be represented in the sequence listing?

The sequence must be included in a sequence listing as:

attcatacgcactatacgcactatacgcactatacgcactgtac (SEQ ID NO: 22)

Relevant ST.26 paragraphs: 7(a) and 13

Example 7(a)-5: Nonconventional nucleotide symbols I

A patent application describes the following sequence:

5' GATC-β-β-β-β-GTAC 3'

The explanation of the sequence in the disclosure further indicates that "β" consists of the sequence 5' ATACGCACT 3'.

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The enumerated sequence uses the nonconventional symbol "β". The explanation of the sequence in the disclosure must be consulted to determine the meaning of "β" (see Introduction to this document).

Consultation of the disclosure indicates that "β" is equivalent to 5' ATACGCACT 3'. Thus, the "β" is a nonconventional symbol used to represent a sequence of nine specifically defined, conventional symbols. Accordingly, the sequence must be interpreted as though it were disclosed using the equivalent conventional symbols:

5' GATC-ATACGCACT-ATACGCACT-ATACGCACT-ATACGCACT-GTAC 3'

The enumerated sequence has 44 specifically defined nucleotides and is required by ST.26 paragraph 7(a) to be included in a sequence listing.

Question 3: How should the sequence(s) be represented in the sequence listing?

The sequence must be included in a sequence listing as:

gatcatacgcactatacgcactatacgcactatacgcactgtac (SEQ ID NO: 23)

Relevant ST.26 paragraphs: 7(a) and 13

Example 7(a)-6: Nonconventional nucleotide symbols II

A patent application describes the following sequence:

5' GATC-β-β-β-β-GTAC 3'

The explanation of the sequence in the disclosure further indicates that "β" is equal to adenine, inosine, or pseudouridine.

Question 1: Does ST.26 require inclusion of the sequence(s)?

NO

The enumerated sequence uses the nonconventional symbol "β". The explanation of the sequence in the disclosure must be consulted to determine the meaning of "β" (see Introduction to this document).

Consultation of the disclosure indicates that "β" is equivalent to adenine, inosine, or pseudouridine. The only conventional symbol that can be used to represent "adenine, inosine, or pseudouridine" is "n"; therefore, the "β" is a nonconventional symbol used to represent the conventional symbol "n". Accordingly, the sequence must be interpreted to have four "n" symbols (shown as "N" below) in place of the four "β" symbols:

5' GATC-N-N-N-N-GTAC 3'

The enumerated sequence has only eight specifically defined nucleotides and is not required by ST.26 paragraph 7(a) to be included in a sequence listing.

Question 2: Does ST.26 permit inclusion of the sequence(s)?

~~NO~~**YES**

ST.26 paragraph 8 permits inclusion of sequences with fewer than ten specifically defined nucleotides. Therefore, t~~T~~he enumerated sequence, 5' GATC-N-N-N-N-GTAC 3' ~~must not~~may be included in a sequence listing.

~~However, a disclosed alternative sequence may be included in a sequence listing if at least 2 of the "n" symbols are replaced by adenine, resulting in a sequence with at least 10 or more specifically defined nucleotides.~~

Question 3: How should the sequence(s) be represented in the sequence listing?

The sequence should be represented in the sequence listing as:

gatcnnnngtac (SEQ ID NO: 109)

The "n" residues at positions 5-8 should be further annotated in a feature table using the feature key "misc_difference" and the mandatory qualifier "note" with a value indicating that "n" is adenine, inosine or pseudouridine. Since two alternatives are modified nucleotides, then the feature key "modified_base" together with the qualifier "mod_base" should also be used. The value for the "mod_base" qualifier ~~should~~must be "OTHER." Two note qualifiers are required; one with the value "i" and the other with the value "p".

~~One possible permitted representation is:~~

~~gatcaaaagtac (SEQ ID NO: 24)~~

~~In the above example, the four adenine nucleotides that replace the β symbols should be annotated to note that these positions could be substituted with inosine or pseudouridine.~~

~~The feature key "misc_difference" should be used with a feature location 5-8 and a qualifier "note" with the value, e.g., "A nucleotide in any of positions 5-8 may be replaced with inosine or pseudouridine". Since these alternatives are modified nucleotides, then the feature key "modified_base" together with the qualifier "mod_base" would be required. The value for the "mod_base" qualifier can be "OTHER" with a "note" qualifier and the value of "i or p".~~

~~Other permutations are possible.~~

~~**CAUTION:** The preferred representation of the sequence indicated above is directed to the provision of a sequence listing on the filing date of a patent application. The same representation may not be applicable to a sequence listing provided subsequent to the filing date of a patent application, since consideration must be given to whether the information provided could be considered by an IPO to add subject matter to the original disclosure.~~

Relevant ST.26 paragraphs: 7(a), 8, 13, and 17

Example 7(a)-7: Inverted nucleotides I

A patent application discloses the following single stranded DNA sequence:

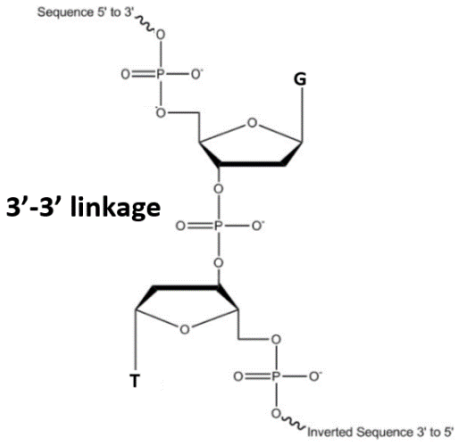
5'attgactaagtgttccccattgact5'

Wherein the directionality of the sequence changes within the strand due to a 3' to 3' reversed linkage between residues 12 and 13. The underlined portion of the sequence is oriented 3' to 5' from left to right.

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The first 12 residues are depicted in the standard 5' to 3' orientation. The “g” at position 12 is linked to the “t” in position 13 via a 3' to 3' reversed linkage:



The remainder of the molecule, depicted in positions 13 through 25 are in the opposite orientation – 3’ to 5’. ST.26 paragraph 11 requires that a nucleotide sequence be represented in the 5’ to 3’ direction from left to right.

Therefore, to properly represent this molecule in the sequence listing, it must be represented by two sequences – one sequence for positions 1 through 12, and a second for positions 13 through 25. Each portion of the sequence contains ten or more “specifically defined” nucleotides, and as required by ST.26 paragraph 7(a), must be included in a sequence listing.

Question 3: How should the sequence(s) be represented in the sequence listing?

Positions 1-12 must be included in the sequence listing as:

attgactaagtg (SEQ ID NO: 99)

Position 12 should be described in a feature table using the feature key “misc_feature” and the qualifier “note” with a value indicating the residue is connected to an inverted nucleotide sequence through a 3’-3' phosphodiester bond to a thymidine 3' monophosphate at position 13 of the sequence tcagttacccctt.

Positions 13-25 must be included in the sequence listing as:

tcagttacccctt (SEQ ID NO: 100)

Note that this sequence is in the reversed orientation with respect to how it was depicted in the original disclosure, such that it is now oriented 5’ to 3’, from left to right. Position 13 should be described in a feature table using the feature key “misc_feature” and the qualifier “note” with a value indicating the residue is connected to an inverted nucleotide sequence through a 3'-3' phosphodiester bond to a guanosine 3'- monophosphate at position 12 of sequence attgactaagtg.

Relevant ST.26 paragraphs: Paragraphs 7(a), 11

Example 7(a)-8: Inverted Nucleotides II

A patent application discloses the following DNA sequence:

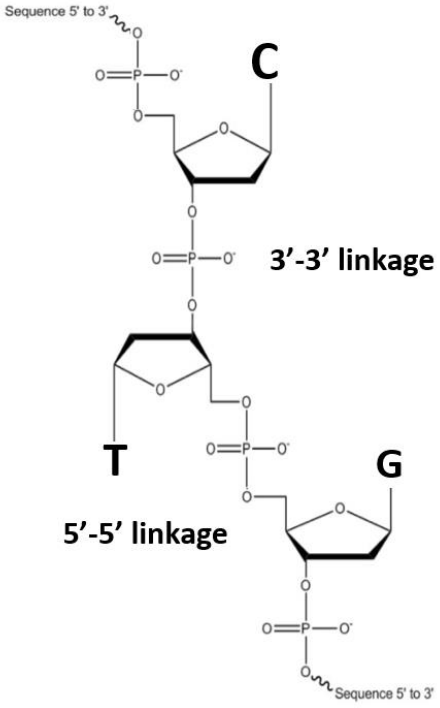
5'-attgactaagtgc**t**gcccattgact-3'

Wherein the underlined thymine residue (position 14) is an inverted nucleotide that is connected to the cytosine via a 3'-3' phosphodiester bond and to the guanine via a 5' to 5' phosphodiester bond.

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The inverted thymidine at position 14 interrupts the 5' to 3' directionality of the sequence by introducing a 3'-3' bond between residues 13 and 14 and a 5' -5' bond between residues 14 and 15:



The inverted thymidine links the first portion of the sequence, residues 1-13, and the second portion of the sequence, residues 15-25. Each portion of the sequence contains at least 10 enumerated and specifically defined nucleotides. Thus, each portion of the sequence must be included in a sequence listing as required by ST.26 paragraph 7(a). The single thymidine linking the two portions of the sequence cannot be included in the sequence listing as a separate sequence because it is not a sequence of at least 10 specifically defined nucleotides.

Question 3: How should the sequence(s) be represented in the sequence listing?

The inverted thymidine at position 14 interrupts the 5' to 3' directionality of the sequence by introducing a 3'-3' bond between residues 13 and 14 and a 5' -5' bond between residues 14 and 15. ST.26 paragraph 11 requires that a nucleotide sequence be represented in the 5' to 3' direction from left to right. Therefore, to properly represent this molecule in the sequence listing, it must be represented by two sequences – a first sequence for residues 1 through 13 and a second sequence for residues 15 through 25.

Positions 1-13 must be included in a sequence listing as:

attgactaagtgc (SEQ ID NO: 101)

Position 13 should be described in a feature table using the feature key “misc_feature” and the qualifier “note” with a value indicating the residue is connected ~~to another sequence~~ via a 3'-3' phosphodiester bond to a thymidine 3'-monophosphate that is in turn connected ~~to another sequence~~ via a 5'-5' phosphodiester bond to the g residue at position 1 of the sequence gcccattgact.

Positions 15-25 must be included in a sequence listing as:

gcccattgact (SEQ ID NO: 102)

Position 1 should be described in a feature table using the feature key “misc_feature” and the qualifier “note” with a value indicating the residue is connected ~~to another sequence~~ via a 5'-5' phosphodiester bond to a thymidine 3'-monophosphate that is in turn connected ~~to another sequence~~ via a 3'-3' phosphodiester bond to the c residue at position 13 of the sequence attgactaagtgc.

Relevant ST.26 paragraphs: Paragraphs 7(a), 11

Paragraph 7(b) – Amino Acid sequences required in a sequence listing

Example 7(b)-1: Four or more specifically defined amino acids

XXXXXXXXDXXXXXXXXXXFXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXAXXXXXXXXXXXXXXXXXXXXGXXXXX

Where X = any amino acid

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The enumerated peptide contains four specifically defined amino acids. The symbol "X" is used conventionally to represent the remaining amino acids as any amino acid (see Introduction to this document).

Because there are four specifically defined amino acids, i.e., Asp, Phe, Ala and Gly, ST.26 paragraph 7(b) requires that the sequence be included in a sequence listing.

Question 3: How should the sequence(s) be represented in the sequence listing?

The sequence must be represented as:

XXXXXXXXDXXXXXXXXXXFXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXAXXXXXXXXXXXXXXXXXXXXGXXXXX (SEQ ID NO: 25)

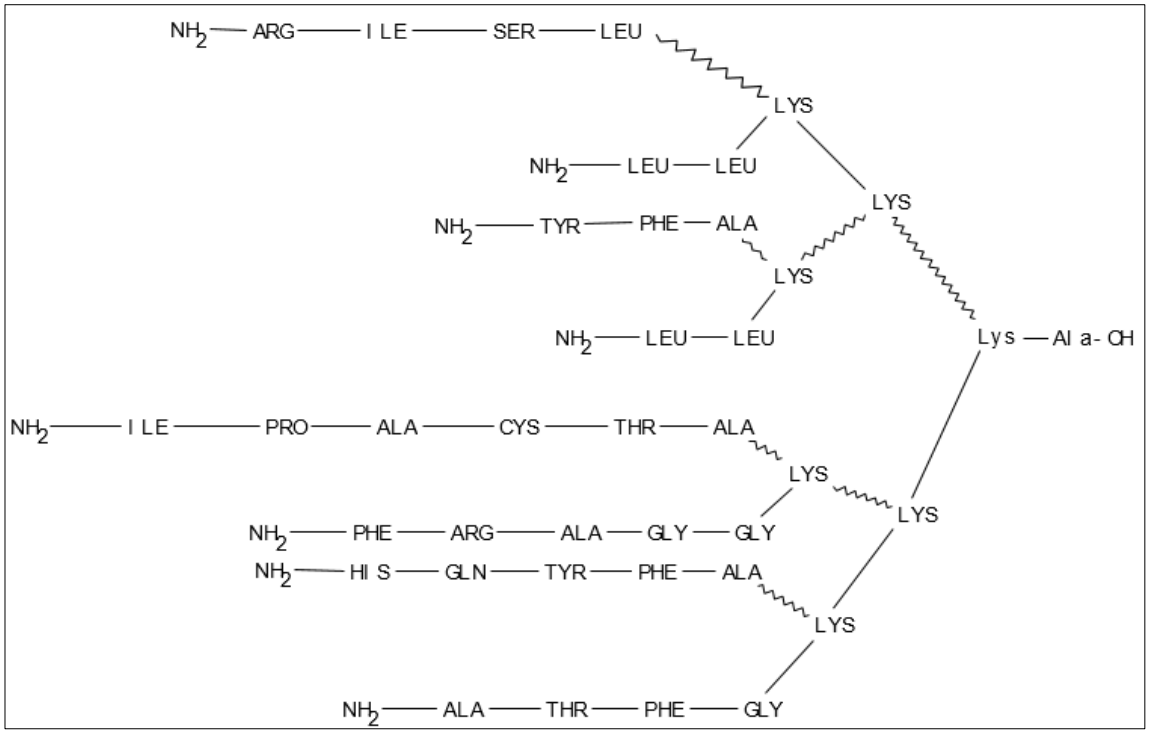
According to paragraph 27, "X" will be construed as any one of the unmodified L-alpha amino acids: "A", "R", "N", "D", "C", "Q", "E", "G", "H", "I", "L", "K", "M", "F", "P", "O", "S", "U", "T", "W", "Y", or "V", except where it is used with a further description in the feature table. ~~Since~~ "X" in SEQ ID NO: 25 represents "any amino acid", which is broader in scope than the default definition of "X" given in paragraph 27, since "any amino acid" encompasses modified or other amino acids. Therefore, the "X" residues in this sequence ~~it~~ must be annotated with the feature key VARIANT and a note qualifier with the value, "X can be any amino acid".

Where practicable, each "X" should be annotated individually. However, a region of contiguous "X" residues~~, or a multitude of "X" residues dispersed throughout the sequence,~~ may be jointly described with the feature key VARIANT using the syntax "x..y" as the location descriptor, where x and y are the positions of the first and last "X" residues, and a note qualifier with the value, "X can be any amino acid".

Relevant ST.26 paragraph(s): 7(b)~~, 8~~ and 27

Example 7(b)-2: Branched amino acid sequence I

The application describes a branched sequence where the ~~Lysine~~ lysine residues are used as a scaffolding core to form eight branches to which multiple linear peptide chains are attached. Lysine is a dibasic amino acid, providing it with two sites for ~~peptide~~amide-bonding. The ~~peptide~~ branched sequence is illustrated as follows:



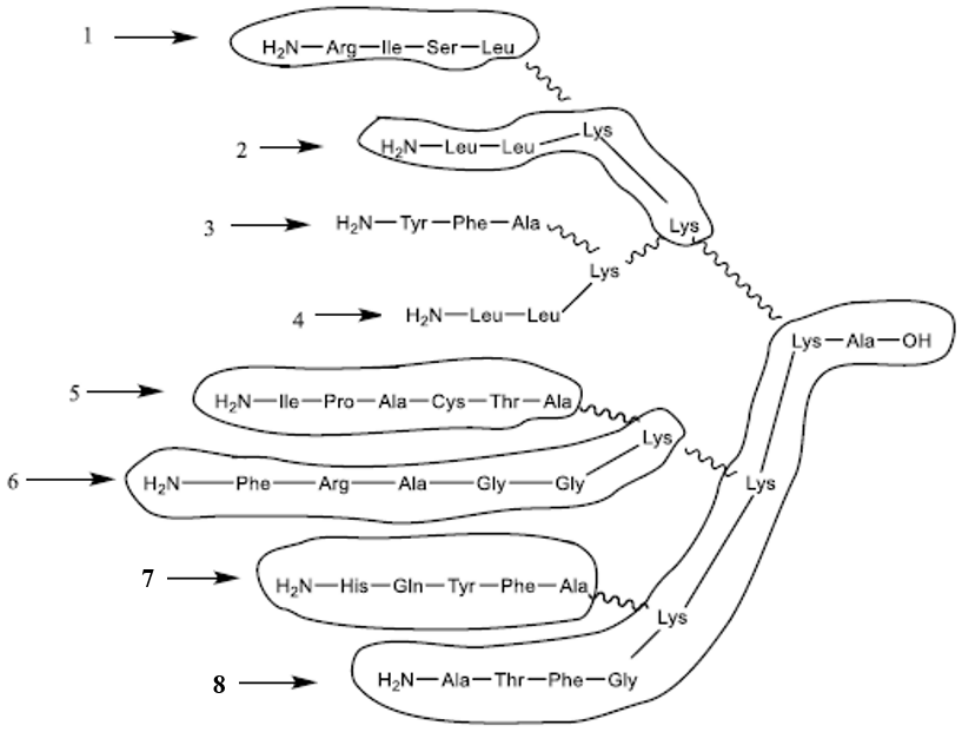
In the above branched peptide, the bonds between lysine and ~~another~~ an adjacent amino acid depicted by ——— represent an amide linkage between the terminal amine of the lysine and the carboxyl end of the bonded amino acid. The bonds depicted by ∿∿∿ represent an amide linkage between the side chain amine of the lysine and the carboxyl end of the bonded amino acid.

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The example discloses a branched sequence where the lysine residues are used as a scaffolding. Since the illustration distinguishes between backbone amide linkages (———) and side chain amide linkages (∿∿∿), the linear regions of the branched sequence that form each backbone are apparent. Paragraph 7(b) requires that ~~the~~ an unbranched or linear region of the sequence, containing four or more specifically defined amino acids, wherein the amino acids form a single peptide backbone, be included in a sequence listing.

~~In the above example, the linear regions of the branched peptide that have four or more specifically defined amino acids are encircled~~This branched sequence is comprised of 8 linear peptides; the linear peptides that have four or more amino acids are encircled:



Peptides 1 and ~~3-6~~ 5-8 contain four or more specifically defined amino acids. Therefore, ST.26 paragraph 7(b) requires inclusion of peptides 1 and ~~3-6~~ 5-8 in a sequence listing.

Peptide 2 contains two specifically defined amino acids (Leu-Leu). The two Lys residues at positions 3 and 4 are modified by virtue of the amide linkage between their side chain amines and the carboxyl end of the bonded amino acid. According to ST.26 paragraph 29, modified amino acids should be represented in the sequence as the corresponding unmodified amino acids whenever possible. Therefore, the two modified Lys residues should be represented by "K" in the sequence listing and not "X". Consequently, peptide 2 should be included in the sequence listing as "LLKK."

Peptides ~~7~~3 and ~~8~~4 each contain only 3 amino acids; therefore, they are not required to be included in a sequence listing.

~~ST.26 paragraph 7(b) requires inclusion of peptides 1-6 above in a sequence listing.~~

~~Peptides which are not required to be included in the sequence listing are:~~

~~YFA~~

~~LLK~~

Question 2: Does ST.26 permit inclusion of the sequence(s)?

~~NO~~**YES**

According to paragraph 8, a sequence listing ~~must not~~may include ~~any~~ sequences having fewer than four specifically defined amino acids.

~~The p~~Peptides 3 and 4 ~~3 and 4, YFA and LLK2, 7 and 8, respectively,~~ each contain ~~only three~~less than four specifically defined amino acids. ~~and therefore, they must not be included~~~~their inclusion~~Therefore their inclusion ~~may be included~~ in a sequence listing as separate sequences with their own sequence identification numbers is optional.

Question 3: How should the sequence(s) be represented in the sequence listing?

All of the modified lysine residues in the above peptides should be represented with the symbol “K” in the sequence and not "X", in accordance with the recommendation in ST.26 paragraph 29.

Peptides 1, and 5-8 ~~-6~~ must be ~~represented~~ included in a sequence listing with separate sequence identifiers and should be represented as follows:

RISL (SEQ ID NO: 26)

~~LLKK (SEQ ID NO: 27)~~

IPACTA (SEQ ID NO: 28)

FRAGGK (SEQ ID NO: 29)

HQYFA (SEQ ID NO: 30)

ATFGKKKA (SEQ ID NO: 31)

In addition, it is highly recommended that peptide 2 ~~is~~be included in the sequence listing, with its own sequence identifier, and represented as follows:

LLKK (SEQ ID NO: 27)

~~Peptides 3 and 4 may be included in the sequence listing and represented as follows:~~

~~YFA (SEQ ID NO: xx)~~

~~LLK (SEQ ID NO: xx)~~According to ST.26, paragraph 30, the modified lysine residues in each sequence must be annotated using the feature key “SITE” together with the qualifier “note.” The value of the “note” qualifier should describe that the side chain of the lysine is linked via an amide linkage to another sequence. In addition, each sequence in the~~The~~ branched structure may be annotated using the feature key “SITE” and the mandatory qualifier “note” with the value e.g., “This sequence is one part of a branched amino acid sequence”. ~~According to ST.26 paragraph 30, SEQ ID Nos 27, 29, and 31, must include an annotation for each lysine to indicate that it is a modified amino acid, using the feature key “SITE” together with the qualifier “note” describing that the side chain of the lysine is linked via an amide linkage to another sequence. Each of the SEQ ID Nos 26, 28, and 30 should include an annotation to indicate that the C-terminal amino acid is linked to another sequence, using the feature key “SITE” together with the qualifier “note”.~~

Peptides 3 and 4 may be included in the sequence listing and represented as follows:

YFA (SEQ ID NO: 110)

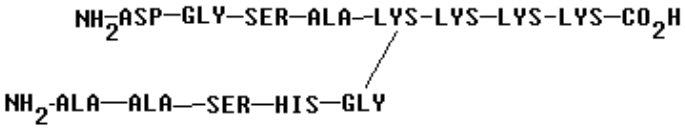
LLK (SEQ ID NO: 111)

These sequences should be annotated in a similar way as explained above for SEQ ID 26-31.

Relevant ST.26 paragraph(s): 7(b), 8, 26, 29, 30, and 31

Example 7(b)-3: Branched amino acid sequence II

Peptide of the following sequence:

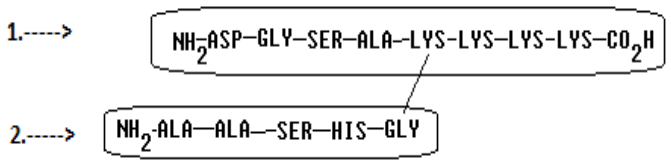


The linkage between the terminal Glycine residue in the lower sequence and the Lysine in the upper sequence is through an amide bond between the carboxy terminus of the Glycine and the amino terminal side chain of the Lysine.

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

~~The~~ An unbranched or linear region of a sequence, containing four or more specifically defined amino acids, must be included in a sequence listing. In the above example, the linear regions of the branched peptide that have more than four amino acids are:



ST.26 paragraph 7(b) requires inclusion of sequences 1 and 2 in a sequence listing.

Question 3: How should the sequence(s) be represented in the sequence listing?

The lysine residue in position 5 of sequence 1 is modified by virtue of the amide linkage between the lysine side chain amine and the carboxyl end the C-terminal glycine. According to ST.26 paragraph 29, modified amino acids should be represented in the sequence as the corresponding unmodified amino acids whenever possible. Therefore, the modified lysine residue should be represented by "K" in the sequence.

Accordingly, s~~S~~equences 1 and 2 ~~must~~ should be represented ~~with separate sequence identifiers~~ as follows:

DGSAKKKK (SEQ ID NO: 32)

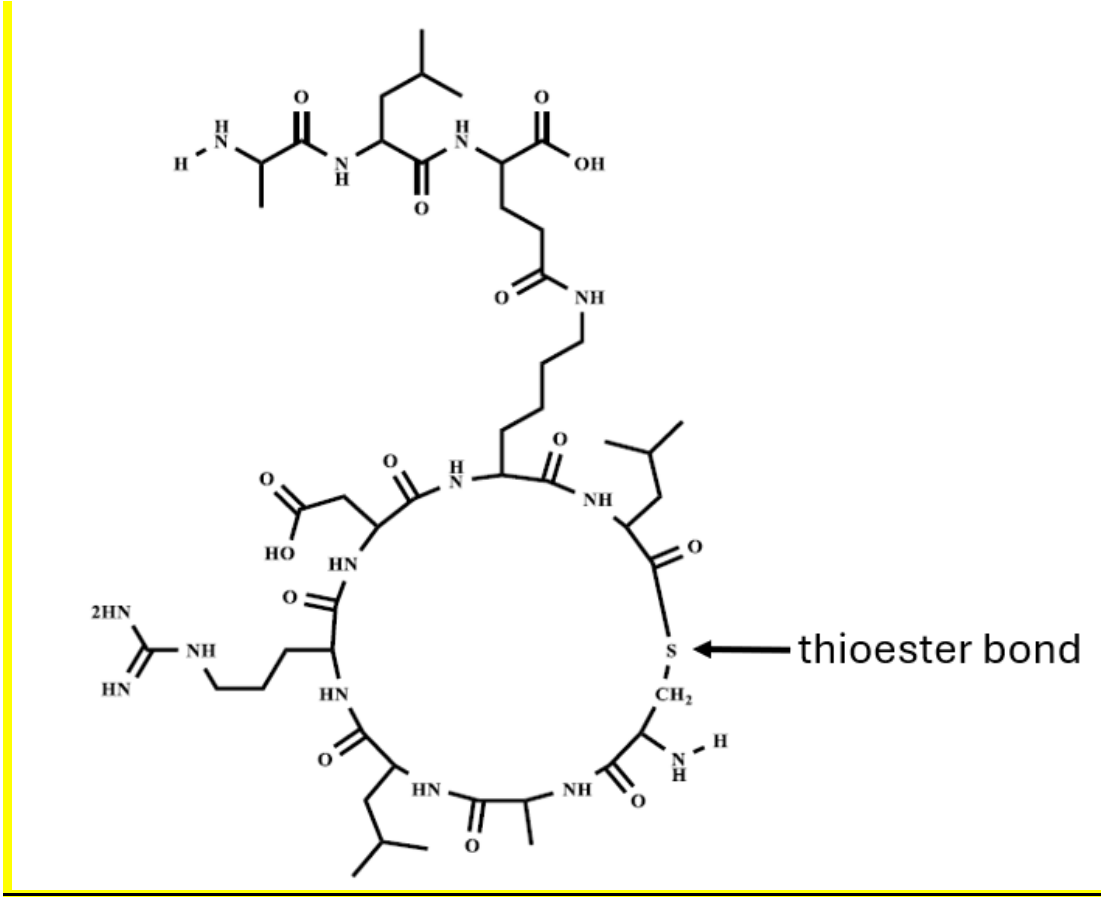
AASHG (SEQ ID NO: 33)

The sequence DGSAKKKK must include an annotation to indicate that the lysine in position number 5 is a modified amino acid, using the feature key "SITE" together with the qualifier "note" describing that the side chain of the lysine is linked via an amide linkage to another sequence. The sequence AASHG should include an annotation to indicate that the glycine in position number 5 is linked to another sequence using the feature key "SITE" together with the qualifier "note".

Relevant ST.26 paragraph(s): 7(b), 26, 29, 30, and 31

Example 7(b)-4: Cyclic peptide containing a branched amino acid sequence I

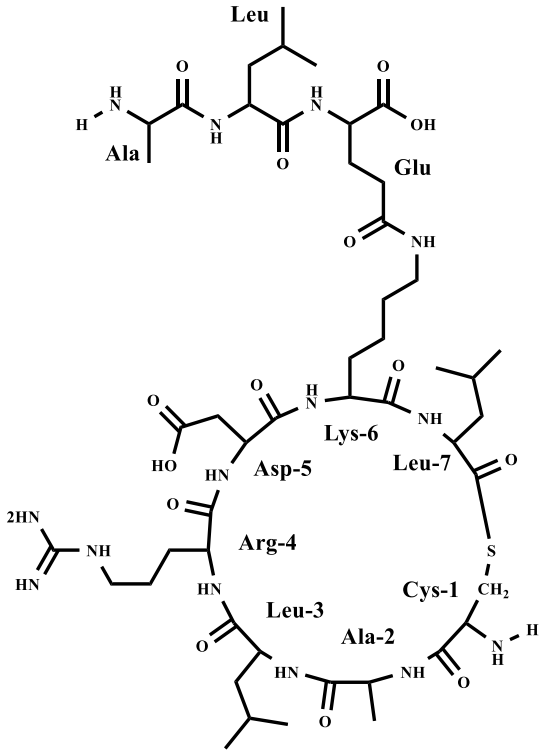
A patent application discloses the following structure:



The Cysteine and Leucine in the cyclic structure are linked ~~through~~ via a thioester bond between the side chain of the Cys and carboxy terminus of the Leu.

Question 1: Does ST.26 require inclusion of the sequence(s)?

The structure shown is a branched cyclic amino acid sequence which contains the following amino acids:



Since the side chain of the Cys and carboxy terminus of the Leu are involved in the cyclization, the N-terminus of the cyclic peptide is located at Cys-1. The side chain of the Lys in position 6 of the cyclic structure is linked through an amide bond with the side chain of the Glu at the C terminus of the three amino acid peptide Ala-Leu-Glu to form a branched sequence.

YES – the cyclic region of the peptide

ST.26 paragraph 7(b) requires that the linear region of a branched sequence containing four or more specifically defined amino acids, wherein the amino acids form a single peptide backbone, must be included in a sequence listing. In the above example, the cyclic region of the branched peptide has more than four specifically defined amino acids, and therefore, must be included in a sequence listing.

NO – the tripeptide branch of the peptide

The tripeptide branch Ala-Leu-Glu is not required to be in the sequence listing.

Question 2: Does ST.26 permit inclusion of the sequence(s)?

~~NO~~ **YES**

According to paragraph 8, a sequence listing ~~must not~~may include any sequences having fewer than four specifically defined amino acids.

The tripeptide branch contains only three specifically defined amino acids and therefore, its inclusion ~~must not be included~~ in a sequence listing as a separate sequence with its own sequence identification number is optional.

Question 3: How should the sequence(s) be represented in the sequence listing?

While this example illustrates a peptide that is circular in configuration, the ring does not consist solely of amino acid residues in peptide linkages, as indicated in paragraph 25. Since the cyclization of the ~~amino acid sequence~~peptide occurs through the backbone carboxyl group of Leu and the side chain of ~~cysteine (~~Cys~~) and the carboxy terminus of the leucine (Leu)~~, the ~~cysteine~~ Cys is most like an N-terminal residue and must be assigned position number 1 within the cyclic region of the peptide.

The Lys in position 6 of the cyclic region is modified by virtue of the amide linkage between its side chain amine and the side chain carboxyl group of Glu of the tripeptide branch, Ala-Leu-Glu. According to ST.26 paragraph 9, modified amino acids should be represented in the sequence as the corresponding unmodified amino acids where possible. Therefore, this modified Lys residue should be represented by “K” in the sequence listing, and not “X”.

Accordingly, the sequence ~~must~~ should be represented as:

CALRDKL (SEQ ID NO: 90)

As indicated in the figure above, the ~~amino acid sequence~~peptide is cyclized through a thioester conjugation between the ~~cysteine~~ Cys side chain and the carboxy terminus of ~~the leucine~~Leu. The feature key “SITE” must be used to describe the modified ~~cysteine~~Cys, which forms the intrachain linkage with ~~leucine~~Leu. The value of the feature location element is the residue numbers of the cross-linked amino acids in “x..y” format, i.e., “1..7”. The mandatory qualifier “note” should indicate the nature of the linkage, e.g., “cysteine leucine thioester (Cys-Leu)”, to specify that Cys-1 and Leu-7 are linked through a thioester bond. Further, the ~~lysine~~ Lys in position number 6 must be annotated to indicate that it is modified, by using the feature key “SITE” together with the mandatory qualifier “note”, where the qualifier value describes that the ~~lysine~~ Lys side chain links to the tripeptide ALE.

In addition, if the tripeptide is included in the sequence listing, it should be represented as:

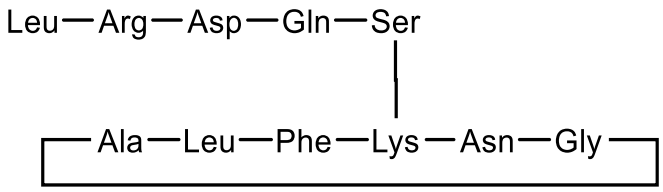
ALE (SEQ ID NO: 112)

The “E” residue at position 3 should be annotated with a feature key “SITE” together with a mandatory qualifier “note” to indicate that it is attached to the “K” residue at position 6 of the cyclic peptide of sequence CALRDKL.

Relevant ST.26 paragraphs: 7(b), 8, 25, 26, 29, 30, 31, 66(c), and 70

Example 7(b)-5: Cyclic peptide containing a branched amino acid sequence II

A patent application discloses the following branched cyclic peptide:

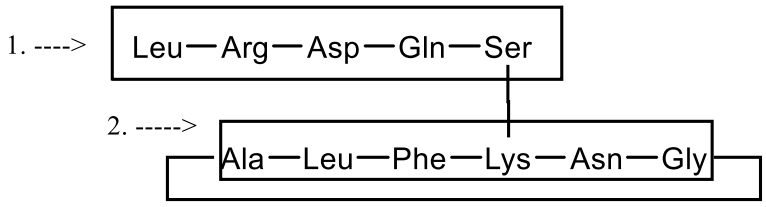


The Ser and the Lys are linked through an amide bond between the carboxy terminus of the serine and amine in the side chain of the Lys.

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

Paragraph 7(b) requires inclusion of any sequence that contains four or more specifically defined amino acids and which can be represented as a linear region of a branched sequence in a sequence listing. In the above example, the peptide contains a cyclic region wherein the amino acids are joined by ~~peptide~~ amide bonds, and a branched region which is joined to a side chain of the Lys in the cyclic region. The regions of this branched peptide which can be represented as linear and which contain four or more specifically defined amino acids are:



ST.26 requires inclusion of sequences 1 and 2 of this cyclic branched peptide in a sequence listing, each with ~~their~~ its own sequence identification number.

Question 3: How should the sequence(s) be represented in the sequence listing?

Sequence 1 must be represented as:

LRDQS (SEQ. ID. NO: 91)

Sequence 1 may be annotated by using the feature key “SITE” together with the qualifier “note” to describe that the serine in position 5 is linked to another sequence through an amide linkage between the backbone carboxyl group of Ser and a side chain of a Lys in the other sequence.

Sequence 2 is a cyclic peptide. Paragraph 25 indicates that when an amino acid sequence is circular in configuration and has no amino and carboxy termini, applicant must choose the amino acid residue in position number 1. Although any amino acid in the sequence could be designated as residue position number 1, in view of the disclosed depiction of the branched cyclic peptide, Ala is appropriately selected as the first residue. The Lys in position 4 is modified by virtue of the amide bond between its side chain and the carboxy end of Ser in Sequence 1. According to ST.26 paragraph 29, modified amino acids should be represented in the sequence as the corresponding unmodified amino acids wherever possible. Therefore, the modified Lys residue should be represented as “K” in the sequence, and not “X”. Accordingly, the sequence ~~may~~ should be represented as:

ALFKNG (SEQ. ID. NO: 92)

Alternatively, any other amino acid in the sequence could be designated as residue position number 1. The ~~sequence~~ Lys in position 4 must be further described using the feature key “SITE” together with the qualifier “note” to describe that the side chain ~~of the Lys in residue position number 4~~ is linked via an amide linkage to another sequence. This side chain linkage modifies the Lys, and according to ST.26 paragraph 30, a modified amino acid must be further described in the feature table. Moreover, a feature key “REGION” and a qualifier “note” should be provided to indicate that the peptide ALFKNG is circular.

Relevant ST.26 paragraphs: 7(b), 25, 26, 30, and 31

Paragraph 11(a) – Double-stranded nucleotide sequence – fully complementary

Example 11(a)-1: Double-stranded nucleotide sequence – same lengths

A patent application describes the following double-stranded DNA sequence:

3′-CCGGTTAACGCTA-5′

5′-GGCCAATTGCGAT-3′

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

Each enumerated nucleotide sequence has more than 10 specifically defined nucleotides. At least one strand must be included in the sequence listing, because the two strands of this double-stranded nucleotide sequence are fully complementary to each other.

Question 2: Does ST.26 permit inclusion of the sequence(s)?

YES

While the sequence of only one strand must be included in the sequence listing, the sequences of both strands may be included, each with its own sequence identification number.

Question 3: How should the sequence(s) be represented in the sequence listing?

The double-stranded DNA sequence must be represented either as a single sequence or as two separate sequences. Each sequence included in the sequence listing must be represented in the 5' to 3' direction and assigned its own sequence identification number.

atcgcaattggcc (top strand) (SEQ ID NO: 34)

and/or

ggccaattgcgat (bottom strand) (SEQ ID NO: 35)

Relevant ST.26 paragraphs: 7(a), **11(a)**, and 13

Paragraph 11(b) – Double-stranded nucleotide sequence - not fully complementary

Example 11(b)-1: Double-stranded nucleotide sequence – different lengths

A patent application contains the following drawing and caption:

```
5′-tagttcattgactaaggctccccattgactaaggcgactagcattgactaaggcaagc-3′
                        ||||||||||||||||
                        gggtaactgantccgc
```

The human gene ABC1 promoter region (top strand) bound by a peptide nucleic acid (PNA) probe (bottom strand), where “n” in the PNA probe is a universal PNA base selected from the group consisting of 5-nitroindole and 3-nitroindole.

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES – the ABC1 promoter region (top strand)

The top strand has more than ten enumerated and “specifically defined” nucleotides and is required to be included in a sequence listing.

YES – the PNA probe (bottom strand)

The bottom strand must also be included in the sequence listing, with its own sequence identification number, because the two strands are not fully complementary to each other.

The individual residues that comprise a PNA or “peptide nucleic acid” are considered modified nucleotides according to ST.26 paragraphs 3(f) and 3(g). Furthermore, ST.26 paragraph 16 states that a modified nucleotide with a nucleobase identical to a nucleobase in an unmodified nucleotide listed in Annex I, Section 1, Table 1 must be represented in the sequence as the corresponding unmodified nucleotide. With the exception of the “n” in position 6, the PNA probe is comprised of (2-aminoethyl)-glycine units linked to nucleobases identical to nucleobases in the unmodified nucleotides listed in Annex I, Section 1, Table 1. Accordingly, each position except for position 6 must be represented by the symbol for the corresponding unmodified nucleotide. Therefore, the PNA probe has ~~bottom strand has~~ more than 10 enumerated and “~~“~~specifically defined”~~”~~ nucleotides and is required to be included in a sequence listing.

Question 3: How should the sequence(s) be represented in the sequence listing?

The top strand must be included in a sequence listing as:

tagttcattgactaaggctccccattgactaaggcgactagcattgactaaggcaagc (SEQ ID NO: 36)

The bottom strand is a peptide nucleic acid and therefore does not have a 3’ and 5’ end. According to paragraph 11, it must be included in a sequence listing “in the direction from left to right that mimics the 5’–end to 3’-end direction.” Therefore, it must be included in a sequence listing as:

cgcctnagtcaatggg (SEQ ID NO: 37)

~~The “organism” qualifier of the feature key “source” must have the value “synthetic construct” and the mandatory qualifier “mol_type” with the value “other DNA”.~~ Each nucleotide in ~~The~~ the bottom strand must be described in a feature table using the feature key “modified_base” and the mandatory qualifier “mod_base” with the abbreviation “OTHER”. A “note” qualifier must be included with the complete unabbreviated name of the modified nucleotide~~.~~s. ~~A~~According to ST.2~~4~~6 paragraph 18, as all of the modified nucleotides in the sequence share the same backbone moiety,the region may be jointly described in a feature table with “1..16” as the location descriptor, the feature key “modified_base”, the mandatory qualifier “mod_base” with the abbreviation “OTHER”and a “note” qualifier with a value that is the most restrictive unabbreviated checmial name that encompasses all of the modified nucleotides in the range, such as “N-(2-aminoethyl) glycine nucleosides”.

~~The~~ Since the “n” residue in position 6 includes two possible nucleobase variations – 5-nitroindole and 3-nitroindole – it must be further described as a variant in a feature table using the feature key “~~modified_base~~misc_difference” and the mandatory qualifier “~~mod_base~~note” with ~~the abbreviation “OTHER”. A~~a “~~note”~~ qualifier value that ~~must be~~ includes~~ed~~ ~~with~~ the complete unabbreviated name of the two possible modified nucleotides: “N-(2-aminoethyl) glycine 5-nitroindole or N-(2-aminoethyl) glycine 3-nitroindole”.

Peptide nucleic acid sequences are not naturally occurring. Therefore, according to ST.26 paragraph 83, the “organism” qualifier of the feature key “source” must have the value “synthetic construct” and the mandatory qualifier “mol_type” must have the value “other DNA.”

Relevant ST.26 paragraphs: 3(g), 7(a), **11(b)**, 17, ~~and~~ 18, and 83.

Example 11(b)-2: Double-stranded nucleotide sequence – no base-pairing segment

A patent application describes the following double-stranded DNA sequence:

```
3′-CCGGTTAGCTTATACGCTAGGGCTA-5′
   |||||||       ||||||||||||
5′-GGCCAATATGGCTTGCGATCCCGAT-3′
```

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

Each strand of the enumerated, double-stranded nucleotide sequence has more than 10 specifically defined nucleotides. Both strands must be included in the sequence listing, each with its own sequence identification number, because the two strands are not fully complementary to each other.

Question 3: How should the sequence(s) be represented in the sequence listing?

The sequence of each strand must be represented in the 5' to 3' direction and assigned its own sequence identification number:

atcgggatcgcatattcgattggcc (top strand) (SEQ ID NO: 38)

and

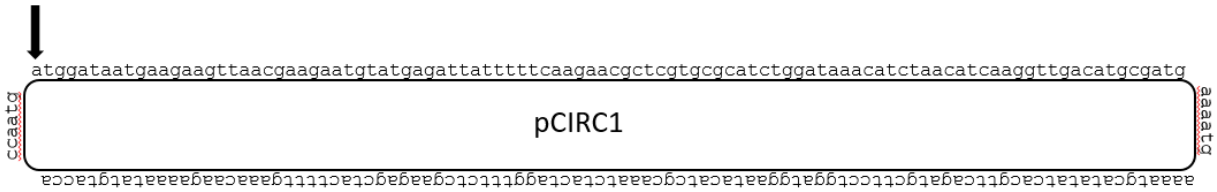
ggccaatatggcttgcgatcccgat (bottom strand) (SEQ ID NO: 39)

Relevant ST.26 paragraphs: 7(a), **11(b)**, and 13

Paragraph 12 – Circular nucleotide sequence

Example 12-1: Circular nucleotide sequence

A patent application contains the following figure, disclosing the DNA sequence of plasmid pCIRC1:



Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The enumerated nucleotide sequence has more than 10 specifically defined nucleotides. Therefore, the sequence must be included in a sequence listing as required by ST.26 paragraph (7)(a).

Question 3: How should the sequence(s) be represented in the sequence listing?

According to ST.26 paragraph 12, when nucleotide sequences are circular in configuration, the applicant must choose the nucleotide in residue position number 1. For the purposes of this example, the “a” residue identified by the arrow in the figure will be used as position 1. However, any residue may be chosen as position 1. With the residue indicated by the arrow as position 1, the sequence should be included in a sequence listing as:

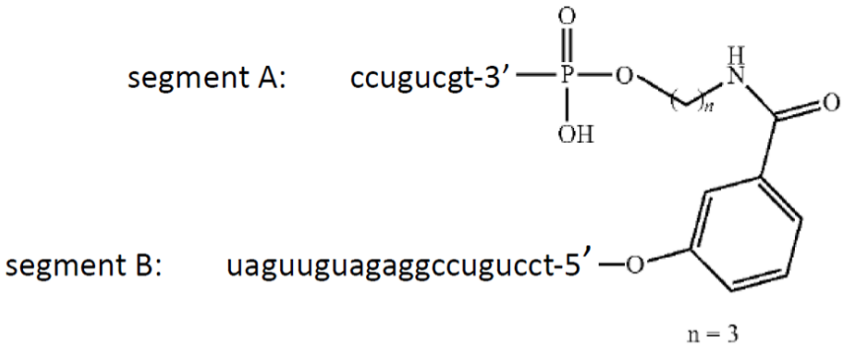
```
atggataatgaagaagttaacgaagaatgtatgagattatttttcaagaacgctcgtgcgcatctggataaacatctaacatca
aggttgacatgcgatgaaaatgaaaatgcatatatcacgttcagatgcttcctggatggaatacatcgcaaatctactaggttt
ctcgaagagctacttttgaaacaagaaaatatgtaccaccaatg
```
(SEQ ID NO: 98)

The sequence should be further described using feature key “misc_feature” with a location of “212^1”, which indicates that the last residue in the sequence, position 212, is linked to residue 1. A “note” qualifier must be included with a value indicating that the molecule is circular.

Relevant ST.26 paragraphs: 7(a), **12**, and Annex I, Section 5, Feature Key 5.15

Paragraph 14 – Symbol "t" construed as uracil in RNA

Example 14-1: The symbol "t" represents uracil in RNA



A patent application describes the following compound:

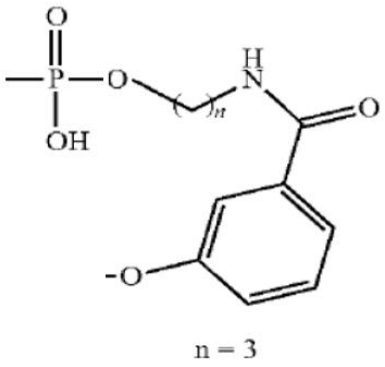
wherein segment A and segment B are RNA sequences.

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES – segment B

NO – segment A

The enumerated sequence contains two segments of specifically defined nucleotides separated by the following "linker" structure:



The linker structure is not a nucleotide according to paragraph 3(g); therefore, each segment must be considered a separate sequence. Segment B contains more than 10 specifically defined nucleotides and ST.26 paragraph 7(a) requires inclusion in a sequence listing. Segment A contains only eight specifically defined nucleotides and therefore is not required to be included in a sequence listing.

Question 2: Does ST.26 permit inclusion of the sequence(s)?

~~NO~~**YES**

Since Segment A contains fewer that 10 specifically defined nucleotides, its inclusion in a sequence listing is optional, as per ST.26 paragraph 8. ~~Segment A contains fewer than 10 specifically defined nucleotides, and as per ST.26 paragraph 8, it's must not be included~~inclusion in a sequence listing ~~is optional~~.

Question 3: How should the sequence(s) be represented in the sequence listing?

Segment B is an RNA molecule; therefore, the element "INSDSeq_moltype" must be "RNA." The symbol "u" must not be used to represent uracil in an RNA molecule in a sequence listing. According to paragraph 14, the symbol

"t" will be construed as uracil in RNA, unless further described in a feature table. Accordingly, segment B must be included in the sequence listing as:

tcctgtccggagatgttgat (SEQ ID NO: 40)

Thymine in RNA is considered a modified nucleotide, i.e. modified uracil, and must be represented in the sequence as "t" and be further described in a feature table, as per paragraph 19 of the Standard. Accordingly, the thymine in position 1 must be further described using the feature key "modified_base", the qualifier "mod_base" with "OTHER" as the qualifier value, and a qualifier "note" with "thymine" as the qualifier value.

The thymine, i.e. modified uracil, in position 1 should also be further described in a feature table using the feature key "misc_feature" and a qualifier "note" with the value e.g., "The 5' phosphate of the thymidine is attached through the linker 3-hydroxybenzamido-N-propyl-3-phosphate to another nucleotide sequence." Where practicable, the other sequence may be directly indicated as the value in the qualifier "note".

If included, segment A should be represented in the sequence listing as follows:

cctgtcgt (SEQ ID NO: 113)

The element "INSDSeq_moltype" must be "RNA". The symbol "u" must not be used to represent uracil in an RNA molecule in a sequence listing. According to paragraph 14, the symbol "t" will be construed as uracil in RNA absent further annotation.

According to ST.26 paragraph 19, tThe thymine in position 8 must be further described using the feature key "modified_base", the qualifier "mod_base" with "OTHER" as the qualifier value, and a qualifier "note" with "thymine" as the qualifier value.

The thymine, i.e. modified uracil, in position 8 should also be further described in a feature table using the feature key "misc_feature" and a qualifier "note" with the value e.g., "The 3' end of the sequence is attached through the linker 3-hydroxybenzamido-N-propyl-3- phosphate to the 5' end of the sequence:

tccuguccggagauguugau ~~(SEQ ID NO: 40)~~

Relevant ST.26 paragraphs: 3(g), 7(a), 8, 13, **14**, 19, and 54

Paragraph 27 – The most restrictive ambiguity symbol should be used

Example 27-1: Shorthand formula for an amino acid sequence

$(GGGz)_2$

Where z is any amino acid.

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The sequence is disclosed as a formula. $(GGGz)_2$ is simply a shorthand way of representing the sequence GGGzGGGz. Conventionally, a sequence is expanded first, and the definition of any variable, i.e. "z", is determined thereafter.

The sequence uses the nonconventional symbol "z". The definition of "z" must be determined from the explanation of the sequence in the disclosure, which defines this symbol as any amino acid (see Introduction to this document). The example does not provide any constraint on "z", e.g., that it is the same in each occurrence.

The peptide in the example has eight enumerated amino acids, six of which are specifically defined glycine residues, and the remaining two are the "z" variable that should be represented in this sequence using the conventional symbol "X". ST.26 paragraph 7(b) requires inclusion of the sequence in a sequence listing as a single sequence with a single sequence identification number.

Note that the sequence is still encompassed by Paragraph 7(b) despite the fact that the enumerated and specifically defined residues are not contiguous.

Question 3: How should the sequence(s) be represented in the sequence listing?

The sequence uses the nonconventional symbol "z", which according to the disclosure is any amino acid. The conventional symbol used to represent "any amino acid" is "X". Therefore, the sequence must be represented as the single expanded sequence:

GGGXGGGX (SEQ ID NO: 41)

According to paragraph 27, "X" will be construed as any one of the unmodified L-alpha-amino acids "A", "R", "N", "D", "C", "Q", "E", "G", "H", "I", "L", "K", "M", "F", "P", "O", "S", "U", "T", "W", "Y", or "V", except where it is used with a further description in the feature table. ~~Since in~~In this example "X" represents "any amino acid", which is broader in scope than the default value of "X" given in paragraph 27, since "any amino acid" encompasses modified or other amino acids. ~~It~~ Therefore, each "X" must be annotated with the feature key VARIANT and a note qualifier with the value, "X can be any amino acid".

~~Where practicable, each "X" should be annotated individually. However, a region of contiguous "X" residues, or a multitude of "X" residues dispersed throughout the sequence, may be jointly described with the feature key VARIANT using the syntax "x..y" as the location descriptor, where x and y are the positions of the first and last "X" residues, and a note qualifier with the value, "X can be any amino acid".~~

~~Further,~~Although the example does not disclose that "z" is the same amino acid in both positions in the expanded sequence~~. However~~, if "z" ~~is~~ were disclosed as the same amino acid in both positions, then ~~a~~ the ~~feature key~~note qualifier value for the "X" in position 4 should state that it can be any amino acid as long as it is the same amino acid as position 8. The "note" qualifier value for the "X" in position 8 should state that it can be any amino acid as long as it is the same amino acid as position 4. ~~"VARIANT" and a qualifier "note" should be provided stating that "X" in position 4 and 8 can be any amino acid, as long as they are the same in both positions.~~

Relevant ST.26 paragraph(s): 3(c), 7(b) and **27**

Example 27-2: Shorthand formula - less than four specifically defined amino acids

A peptide of the formula $(Gly\text{-}Gly\text{-}Gly\text{-}z)_n$

The disclosure further states, that z is any amino acid and

(i) variable n is any length; or

(ii) variable n is 2-100, preferably 3

Question 1: Does ST.26 require inclusion of the sequence(s)?

NO

Consideration of both disclosed embodiments (i) and (ii) of the enumerated peptide of the formula reveals that "n" can be "any length"; therefore, the most encompassing embodiment of "n" is indeterminate. Since "n" is indeterminate, the peptide of the formula cannot be expanded to a definite length, and therefore, the unexpanded formula must be considered.

The enumerated peptide in the unexpanded formula ("n" = 1) provides three specifically defined amino acids, each of which is Gly, and the symbol "z". Conventionally "Z" is the symbol for "glutamine or glutamic acid"; however, the example defines "z" as "any amino acid" (see Introduction to this document). Under ST.26, an amino acid that is not specifically defined is represented by "X". Based on this analysis, the enumerated peptide, i.e., GGGX, does not contain four specifically defined amino acids. Therefore, ST.26 paragraph 7(b) does not require inclusion of this sequence, despite the fact that "n" is also defined as specific numerical values in some embodiments.

Question 2: Does ST.26 permit inclusion of the sequence(s)?

YES

According to paragraph 8, sequences containing fewer than four specifically defined amino acids may be included in a sequence listing. Therefore, the enumerated peptide in the unexpanded formula ("n" = 1), which provides three specifically defined amino acids, may be included in the sequence listing.

In addition or alternatively, the embodiments with specific numerical values~~The example provides a specific numerical value~~ for variable "n," i.e., a lower limit of 2, an upper limit of 100, and an exact value 3~~. Any sequence containing at least four specifically defined amino acids~~ may be included in the sequence listing.

Question 3: How should the sequence(s) be represented in the sequence listing?

According to the Introduction to Annex VI, where the length of a sequence can vary due to copy number variation, the longest embodiment of the sequence is considered the most encompassing. In this example, the longest embodiment that is determinate (i.e., has a definitive value for "n") is where n = 100. ~~A sequence~~ Therefore, the sequence containing 100 copies of GGGX is preferred for inclusion in a sequence listing (SEQ ID NO: 42). ~~A further annotation should~~The sequence should be annotated with the feature key "VARIANT" and a qualifier "note" with a value indicating~~e~~ that up to 98 copies of GGGX could be deleted. Inclusion of ~~further~~ additional specific embodiments that are a key part of the invention is strongly encouraged.

According to paragraph 27, "X" will be construed as any one of the unmodified L-alpha-amino acids "A", "R", "N", "D", "C", "Q", "E", "G", "H", "I", "L", "K", "M", "F", "P", "O", "S", "U", "T", "W", "Y", or "V", except where it is used with a further description in the feature table. ~~Since~~ "X" in SEQ ID NO: 42 represents "any amino acid", which is broader in scope than the default value of "X" given in paragraph 27, since "any amino acid" encompasses modified or other amino acids. Therefore, each "X"~~'~~ must be individually annotated with the feature key VARIANT and a note qualifier with the value, "X can be any amino acid".

~~Where practicable, each "X" should be annotated individually. However, a region of contiguous "X" residues, or a multitude of "X" residues dispersed throughout the sequence, may be jointly described with the feature key VARIANT using the syntax "x..y" as the location descriptor, where x and y are the positions of the first and last "X" residues, and a note qualifier with the value, "X can be any amino acid".~~In addition, or ~~alternatively~~as a less preferred representation, the following sequence may be included in ~~the~~a sequence listing:

GGGX (SEQ ID NO: 118)

"X" should be annotated in the same way as indicated above for SEQ ID NO: 42.

CAUTION: The preferred representation of the sequence indicated above as SEQ ID NO: 42 is directed to the provision of a sequence listing on the filing date of a patent application. The same representation may not be applicable to a sequence listing provided subsequent to the filing date of a patent application, since consideration

must be given to whether the information provided could be considered by an IPO to add subject matter to the original disclosure.

Relevant ST.26 paragraph(s): 3(c), 7(b), 8, 26, and **27**

Example 27-3: Shorthand formula - four or more specifically defined amino acids

A peptide of the formula $(Gly\text{-}Gly\text{-}Gly\text{-}z)_n$

Where z is any amino acid and variable n is 2-100, preferably 3.

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The enumerated peptide of the formula provides three specifically defined amino acids, each of which is Gly, and the symbol "z". Conventionally, "Z" is the symbol for "glutamine or glutamic acid"; however, the description in this example defines "z" as "any amino acid" (see Introduction to this document). Under ST.26, an amino acid that is not specifically defined is represented by "X". Based on this analysis, the enumerated repeat peptide does not contain four specifically defined amino acids. However, the description provides a specific numerical value for variable "n," i.e., a lower limit of 2 and an upper limit of 100. Therefore, the example discloses a peptide having at least six specifically defined amino acids in the sequence GGGzGGGz, which is required by ST.26 to be included in a sequence listing.

Question 3: How should the sequence(s) be represented in the sequence listing?

Since "z" represents any amino acid, the conventional symbol used to represent the fourth and eighth amino acids is "X."

ST.26 requires inclusion in a sequence listing of only the single sequence that has been enumerated by its residues. Therefore, at least one sequence containing any of 2, 3, or 100 copies of GGGX must be included in the sequence listing; however, the most encompassing sequence containing 100 copies of GGGX is preferred (SEQ ID NO: 42) (see Introduction to this document). In the latter case, a further annotation could indicate that up to 98 copies of GGGX could be deleted. Inclusion of two additional sequences containing 2 and 3 copies of GGGX, respectively (SEQ ID NO: 44-45), is strongly encouraged.

According to paragraph 27, "X" will be construed as any one of the unmodified L-alpha-amino acids "A", "R", "N", "D", "C", "Q", "E", "G", "H", "I", "L", "K", "M", "F", "P", "O", "S", "U", "T", "W", "Y", or "V", except where it is used with a further description in the feature table. ~~Since~~ "X" in this example represents "any amino acid", which is broader in scope than the default value of "X" given in paragraph 27, since "any amino acid" encompasses modified or other amino acids. #Therefore, each "X" must be individually annotated with the feature key VARIANT and a note qualifier with the value, "X can be any amino acid".

~~Where practicable, each "X" should be annotated individually. However, a region of contiguous "X" residues, or a multitude of "X" residues dispersed throughout the sequence, may be jointly described with the feature key VARIANT using the syntax "x..y" as the location descriptor, where x and y are the positions of the first and last "X" residues, and a note qualifier with the value, "X can be any amino acid".~~

Further, the example does not disclose that the "z" variable is the same in each of the two occurrences in the expanded sequence. However, if "z" is disclosed as the same amino acid in all locations, then a feature Key VARIANT and a Qualifier note should indicate that "X" in all positions can be any amino acid, as long as they are the same in all locations.

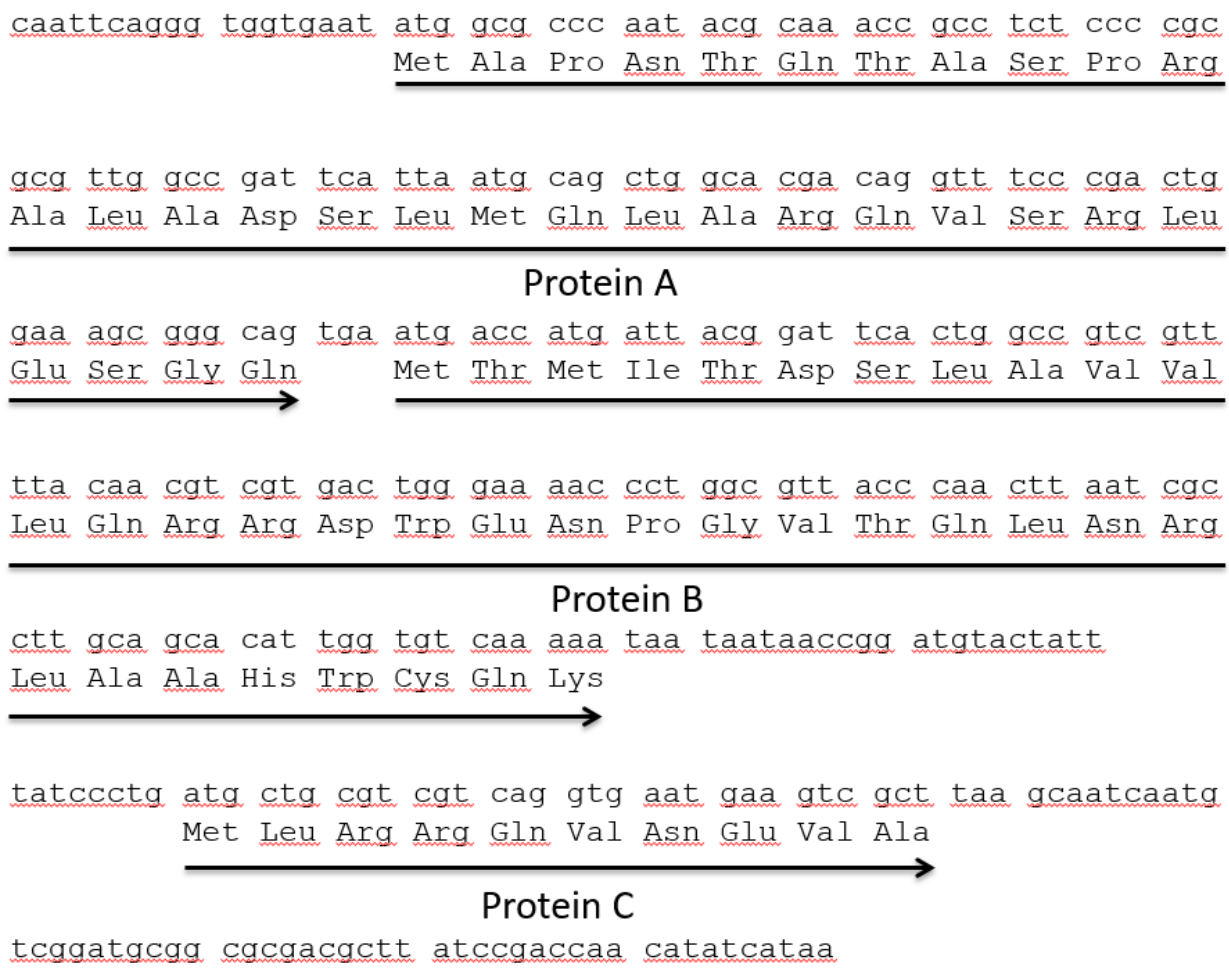
CAUTION: The preferred representation of the sequence indicated above is directed to the provision of a sequence listing on the filing date of a patent application. The same representation may not be applicable to a sequence listing provided subsequent to the filing date of a patent application, since consideration must be given to whether the information provided could be considered by an IPO to add subject matter to the original disclosure.

Relevant ST.26 paragraph(s): 3(c), 7(b), 26, and **27**

Paragraph 28 – Amino acid sequences separated by internal terminator symbols

Example 28-1: Encoding nucleotide sequence and encoded amino acid sequence

A patent application describes the following sequences:



Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The application describes a nucleotide sequence, containing termination codons, which encodes three distinct amino acid sequences.

The enumerated nucleotide sequence contains more than 10 specifically defined nucleotides and must be included in a sequence listing as a single sequence.

Regarding the encoded amino acid sequences, paragraph 28 requires that amino acid sequences separated by an internal terminator symbol such as a blank space, must be included as separate sequences. Since each of "Protein A", "Protein B", and "Protein C" contain four or more specifically defined amino acids, ST.26 paragraph 7(b) requires that each ~~must~~ be included in a sequence listing and ~~must~~ be assigned its own sequence identification number.

Question 3: How should the sequence(s) be represented in the sequence listing?

The nucleotide sequence must be included in a sequence listing as:

caattcagggtggtgaatatggcgcccaatacgcaaaccgcctctccccgcgcgttggccgattcattaatgcagctggccaggcaggtgagcaggctggaaa gcgggcagtgaatgaccatgattacggattcactggccgtcgttttacaacgtcgtgactgggaaaaccctggcgttacccaacttaatcgccttgcagcacattgg tgtcaaaaataataataaccggatgtactatttatccctgatgctgcgtcgtcaggtgaatgaagtcgcttaagcaatcaatgtcggatgcggcgcgacgcttatccg accaacatatcataa (SEQ ID NO: 46)

The nucleotide sequence should further be described using a “CDS” feature key for each of the three proteins and the element INSDFeature_location must identify the location of each coding sequence, including the stop codon. In addition, for each “CDS” feature key, the “translation” qualifier should be included with the amino acid sequence of the protein as the qualifier value. The application does not disclose the genetic code table that applies to the translation (see Annex 1, Section 9, Table 7). If the Standard Code table applies, then the qualifier “transl_table” is not necessary; however, if a different genetic code table applies, then the appropriate qualifier value from Table 7 must be indicated for the qualifier “transl_table”. Finally, the qualifier “protein_id” must be included with the qualifier value indicating the sequence identification number of each of the translated amino acid sequences.

The amino acid sequences must be included as separate sequences, each assigned its own sequence identification number:

MAPNTQTASPRALADSLMQLARQVSRLESGQ (SEQ ID NO: 47)

MTMITDSLAVVLQRRDWENPGVTQLNRLAAHWCQK (SEQ ID NO: 48)

MLRRQVNEVA (SEQ ID NO: 49)

NOTE: See “Example 90-1 Amino acid sequence encoded by a coding sequence with introns” for an illustration of a translated amino acid sequence represented as a single sequence.

Relevant ST.26 paragraphs: 7, 26, **28**, 57, 89-92

Paragraph 29 – Representation of a modified~~n "other"~~ amino acid

Example 29-1: Most restrictive ambiguity symbol for an "other" amino acid

A patent application describes the following sequence:

Ala-Hse-X_1-X_2-X_3-X_4-Tyr-Leu-Gly-Ser

Wherein, X_1= Ala or Gly,

X_2= Ala or Gly,

X_3= Ala or Gly,

X_4= Ala or Gly, and

Hse = Homoserine

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The enumerated peptide contains five specifically defined amino acids. The symbol "X" is used conventionally to represent two amino acids in the alternative (see Introduction to this document).

Because there are at least five specifically defined amino acids, i.e., Ala, Tyr, Leu, Gly and Ser, ST.26 paragraph 7(b) requires that the sequence must be included in a sequence listing.

Question 3: How should the sequence(s) be represented in the sequence listing?

Homoserine at position 2 of the sequence is an alpha amino acid with the side chain -CH_2-CH_2-OH. It is a modified amino acid having a side chain that is not identical to the side chains of any of the L-alpha-amino acid listed in Annex I, Section 3, Table 3. According to ST.26 paragraph 29, a modified amino acid should be represented in the sequence as the corresponding unmodified amino acid whenever possible. The symbol "X" should only be used to represent a modified amino acid when none of the other symbols in Annex I, Section 3, Table 3 is suitable. Accordingly, homoserine may be represented by "X" or the most appropriate amino acid symbol.

~~Paragraph 29 requires any "other" amino acid must be represented by the symbol "X". In the example, the sequence contains the amino acid Hse in position 2 which is not found in Annex I, Section 3, Table 3. Accordingly, Hse is an "other" amino acid and must be represented by the symbol "X".~~

X_1-X_4 are variant positions at residues 3-6, each of which can be A or G. The most restrictive ambiguity symbol for alternatives A or G is "X". Therefore, the sequence may be represented as:

AXXXXXYLGS (SEQ ID NO: 50)

Inclusion of any specific sequences essential to the disclosure or claims of the invention is strongly encouraged, as discussed in the introduction to this document.

According to paragraph 30, Hse must be described using the ~~Since amino acid Hse is not found in Annex I, Section 4, Table 4, a~~ feature key "SITE" and a qualifier "note". Since amino acid Hse is not found in Annex I, Section 4, Table 4, the value of the qualifier "note" must be~~must be provided with~~ the complete, unabbreviated name of homoserine~~ as per ST.26 paragraph 30~~.

According to paragraph 27, because X_1-X_4 represent an alternative of only 2 amino acids, then further description is required. Paragraph 96 indicates that the feature key "VARIANT" should be used with the qualifier "note" and qualifier value "A or G". According to ST.26 paragraph 34, since these positions are adjacent and have the same description, they may be jointly described using the syntax "3..6" as the location descriptor in the element INSDFeature_location.

Relevant ST.26 paragraphs: 3(a), 7(b), 25-27, **29**, 30, 34, 66, 70, 71, and 96-97

Example 29-2: Use of the corresponding unmodified amino acid

A patent application describes the following sequence:

Ala-Hyl-Tyr-Leu-Gly-Ser-Nle-Val-Ser-5ALAOrn

Wherein Hyl = hydroxylysine (post-translational modification of lysine), Nle = nNorleucine, and Orn = ornithine5ALA = δ-Aminolevulinic acid

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The enumerated peptide contains more than four specifically defined amino acids; therefore, the sequence must be included in a sequence listing.

Question 3: How should the sequence(s) be represented in the sequence listing?

The hydroxylysine in position 2, the norleucine in position 7, and the δ-aminolevulinic acidornithine in position 10 are all "modified amino acids". First, we must consider each modified amino acid in view of paragraph 29 to and determine if it should be represented by the corresponding unmodified amino acid or the variable "X" in the sequence. None of hydroxylysine, norleucine, and ornithine contains a side chain that is identical to that of an amino acid listed in Annex I, Section 3, Table 3. Paragraph 29 states that a Accordingly, each modified amino acid "should be represented in the sequence as the corresponding unmodified amino acids whenever possible."

It is up to the discretion of the applicant to decide if a modified amino acid will be represented by the corresponding unmodified residue or the variables "X". However, the following guidance should be taken into account: If an amino acid side chain is modified by the addition of a small moiety, such as methylation or acetylation, and the basic structure of side chain is otherwise preservedthe corresponding unmodified amino acid is generally unchanged, then representation by the unmodified amino acid is recommended. If the modified amino acid side chain is structurally very different from that of the corresponding unmodified amino acid, then representation by an "X" is recommended.

The structure of hydroxylysine is nearly identical to lysine, except that the third carbon in the R-groupside chain is modified with a hydroxyl group. Since the basic structure of the corresponding unmodified lysine residue is intact, it is recommended that hydroxylysine should beis represented in the sequence by lysine ("K" in the sequence), and not by "X".

Norleucine is an isomer of leucine. The R-groupside chain of leucine is a 4-carbon chain, branched at the second carbon. Although nNorleucine also has a 4-carbon R-groupside chain, but it is linear and not branched. Therefore, norleucine isn't simply the result of a modification moiety added to a leucine, but a completely different (although related) structure. Therefore, it is recommended that norleucine isbe represented by an "X" in a sequence listing, and not "L".

δ-Aminolevulinic acidThe structure of arhnithineisornithine is most similar to lysine; lysine has a 4-carbon side chain and ornithine has a 3-carbon side chain. Ornithnine cannot be created by the addition of a small moiety to lysine or any other amino acid is not structurally similar to any of the amino acids listed in Annex I, Table 3. Ttherefore, it is recommended that δ-aminolevulinic acidornithine be is represented by an "X" in a sequence listing and not "K".

Accordingly, the sequence should be included in a sequence listing as:

AKYLGSXVSX (SEQ ID NO: 51)

Paragraph 30 requires the further annotation of each modified amino acid.

Hydroxylysine is a post-translational modification of lysine. Therefore, it must be described using the feature key "MOD_RES" together with a qualifier "note" that describes the modification. Note that "hydroxylysine" is listed in Annex 1, Section 4, Table 4, "List of Modified Amino Acids." Therefore, the value of the qualifier "note" can should contain the abbreviation "Hyl" instead of the complete, unabbreviated name "hydroxylysine."

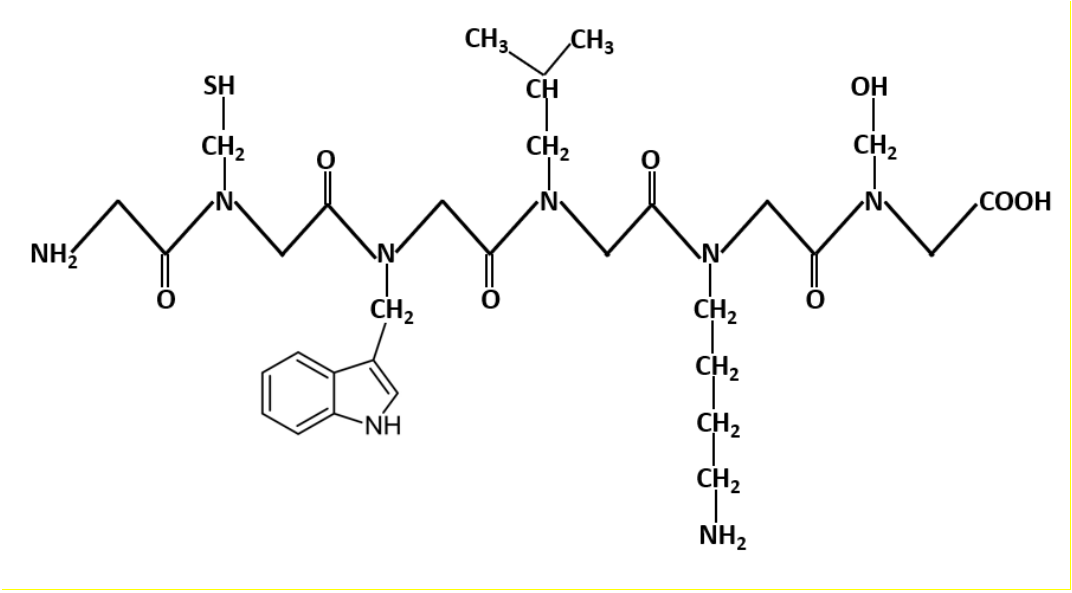
Norleucine is not a post-translationally modified residue, therefore it must be described using the feature key "SITE" together with a qualifier "note" that describes the modification. Note that "norleucine" is also listed in Annex 1, Section 4, Table 4. Therefore, the value of the qualifier "note" can should contain the abbreviation "Nle" instead of the complete, unabbreviated name "norleucine."

~~δ-Aminolevulinic acid~~Ornithine is also not a post-translationally modified residue., T~~t~~herefore it must be described using the feature key "SITE" together with a qualifier "note" that describes the modification. ~~δ-Aminolevulinic acid~~Ornithine is ~~not~~ listed in Annex 1, Section 4, Table 4 with the abbreviation "Orn"., T~~t~~herefore, the value of the qualifier "note" ~~must~~ should contain the ~~complete, unabbreviated name of the modified residue, "δ-aminolevulinic acid~~abbreviation "Orn".~~"~~

Relevant ST.26 paragraphs: 3(a), 3(e), 7(b), 29, and 30

Example 29-3: Peptoid polymer I

A patent application discloses the following peptidomimetic "peptoid" polymer of N-substituted glycine:



Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

N-substituted glycine is encompassed by the definition of an "amino acid" as set forth in paragraph 3(a) of the Standard. Paragraph 29 of the Standard requires representation of a modified amino acid that has a single carbon-containing side chain that is identical to the side chain in an L-alpha-amino acid listed in Annex I, Section 3, Table 3, which is located on the amino nitrogen of the residue, by the symbol of the corresponding unmodified amino acid. In the disclosed peptoid structure:

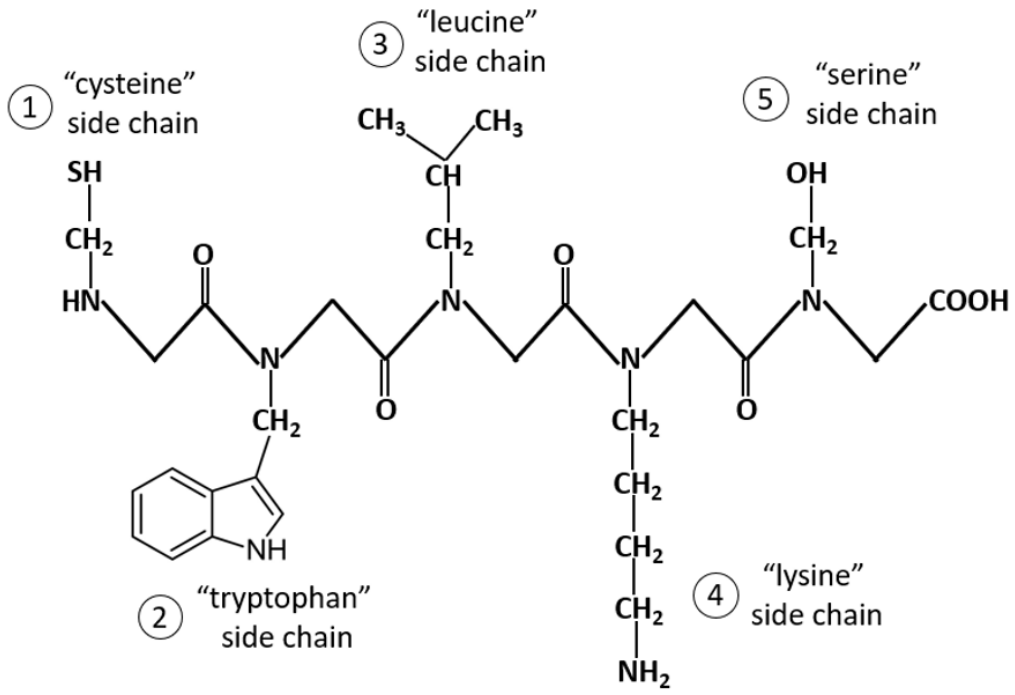
- the side chain attached to the nitrogen of the first residue is identical to the side chain of cysteine;

- the side chain attached to the nitrogen of the second residue is identical to the side chain of tryptophan;

- the side chain attached to the nitrogen of the third residue is identical to the side chain of leucine;

- the side chain attached to the nitrogen of the fourth residue is identical to the side chain of lysine;

- the side chain attached to the nitrogen of the fifth residue is identical to the side chain of serine.



Therefore, the disclosed peptide contains five modified amino acids that are specifically defined, and the sequence must be included in a sequence listing as required by ST.26 paragraph 7(b).

Question 3: How should the sequence(s) be represented in the sequence listing?

The sequence must be included in a sequence listing as:

CWLKS (SEQ ID NO: 114)

Each residue must be described in a feature table using the feature key "SITE" and the mandatory qualifier "note" with a value that describes the residue by its chemical name.

- The "C" in position 1 may be described as "N-(sulfanylmethyl)glycine".
- The "W" in position 2 may be described as "N-(1H-indol-3-ylmethyl)glycine."
- The "L" in position 3 may be described as "N-(isobutyl)glycine."
- The "K" in position 4 may be described as "N-(aminobutyl)glycine."
- The "S" in position 5 may be described as "N-(hydroxymethyl)glycine."

CAUTION: The preferred representation of the sequences indicated above and their annotations is directed to the provision of a sequence listing on the filing date of a patent application. The same representation may not be applicable to a sequence listing provided subsequent to the filing date of a patent application, since consideration must be given to whether the information provided could be considered by an IPO to add subject matter to the original disclosure.

Relevant ST.26 paragraphs: Paragraphs 3(a), 3(e), 7(b), 29, 30, 34

Example 29-4: Peptoid polymer II

An application discloses the following:

Peptide analogues comprising N-substituted glycine residues, such as the sequence NLys-Npa-N4hb-Nnle-NLys-NTrp, are considerably more stable *in vivo* than natural peptides.

The disclosure further indicates that:

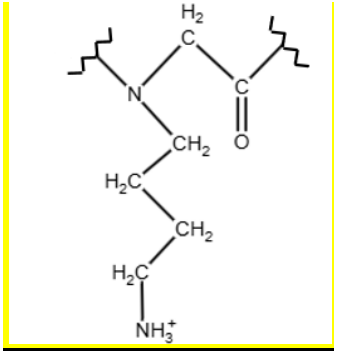
- "NLys" is N-(4-aminobutyl)glycine
- "Npa" is N-(benzyl)glycine
- "N4hb" is N-(4-hydroxybutyl)glycine
- "Nnle" is N-(butyl)glycine
- "NTrp" is N-[1-(indol-3-yl)methyl]glycine

Question 1: Does ST.26 require inclusion of the sequence(s)?

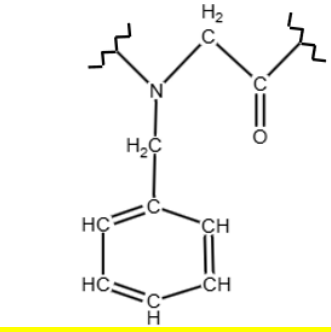
YES

The enumerated sequence comprises six residues having the nonconventional amino acid abbreviations "NLys", "Npa", "N4hb", "Nnle", and "NTrp". The disclosure must be consulted to determine the structure of each amino acid represented by these abbreviations (see Introduction to this document).

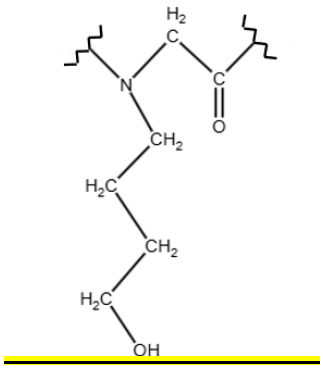
"NLys" is N-(4-aminobutyl)glycine with the structure:



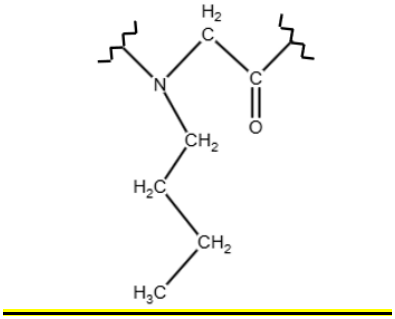
"Npa" is N-(benzyl)glycine with the structure:



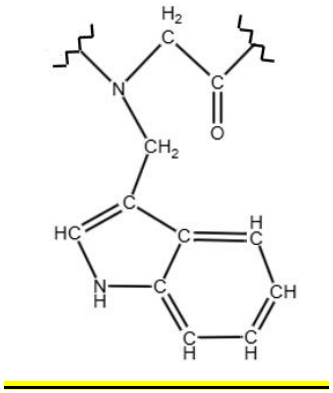
"N4hb" is N-(4-hydroxybutyl)glycine with the structure:



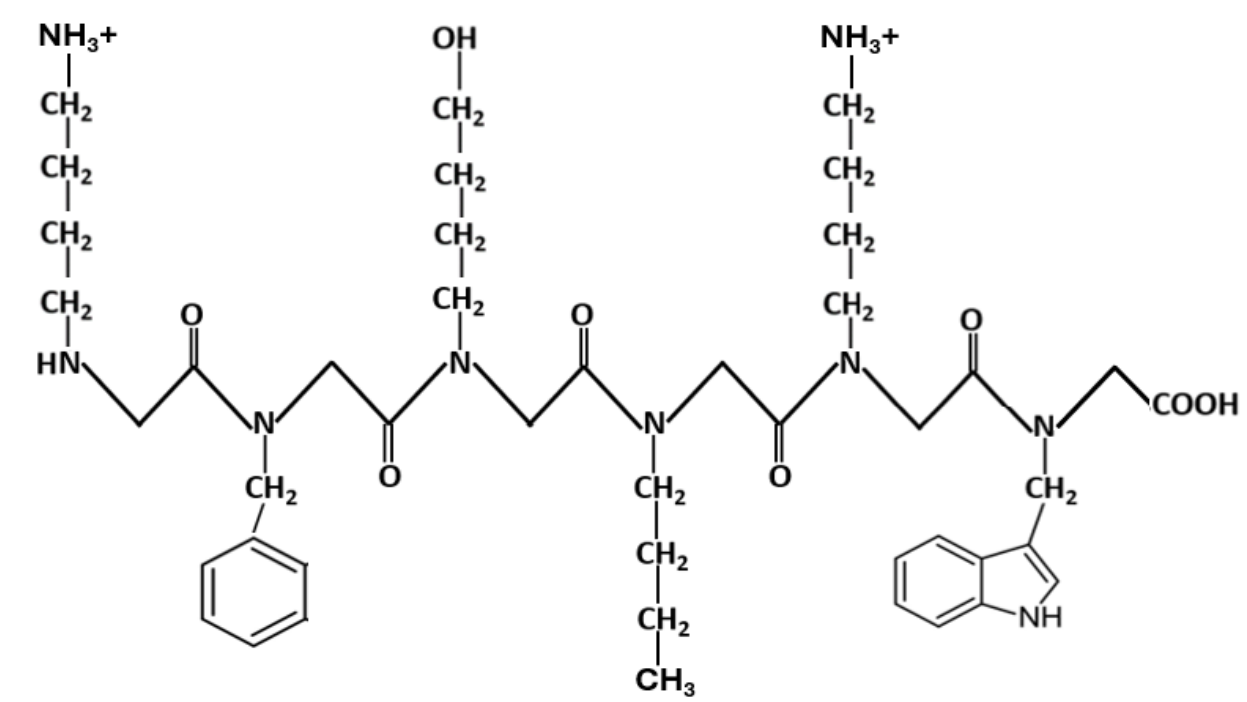
"Nnle" is N-(butyl)glycine with the structure:



"NTrp" is N-[1-(indol-3-yl)methyl]glycine with the structure:



Accordingly, the structure of the disclosed sequence is:



Each residue is an N-substituted glycine, which is encompassed by the definition of an "amino acid" as set forth in paragraph 3(a) of the Standard. Paragraph 29 of the Standard requires the representation of a modified amino acid that has a single carbon-containing side chain that is identical to the side chain in an L-alpha-amino acid listed in Annex I, Section 3, Table 3, which is located on the amino nitrogen of the residue, by the symbol of the corresponding unmodified amino acid. In the disclosed sequence:

- the side chain attached to the nitrogen of the first residue is identical to the side chain of lysine; therefore, this residue must be represented in the sequence by "K";

- the side chain attached to the nitrogen of the second residue is identical to the side chain of phenylalanine; therefore, this residue must be represented in the sequence by "F";

- the side chain attached to the nitrogen of the third residue is NOT identical to the side chains of any of the L-alpha-amino acids listed in Annex I, Section 3, Table 3; therefore, this residue may be represented in the sequence by "X" or the most appropriate amino acid symbol;

- the side chain attached to the nitrogen of the fourth residue is NOT identical to the side chains of any of the L-alpha-amino acids listed in Annex I, Section 3, Table 3; therefore, this residue may be represented in the sequence by "X" or the most appropriate amino acid symbol;

- the side chain attached to the nitrogen of the fifth residue is identical to the side chain of lysine; therefore, this residue must be represented in the sequence by "K";

the side chain attached to the nitrogen of the sixth residue is identical to the side chain of tryptophan; therefore, this residue must be represented in the sequence by "W".

In view of the analysis above, the disclosed sequence contains, minimally, four specifically defined amino acids, and must be included in a sequence listing as required by ST.26 paragraph 7(b).

Question 3: How should the sequence(s) be represented in the sequence listing?

If "X" is deemed the most appropriate symbol for the third and fourth residues, then the sequence must be included in a sequence listing as:

KFXXKW (SEQ ID NO:115)

Each residue must be described in a feature table using the feature key "SITE" and the mandatory qualifier "note" with a value that describes the residue by its chemical name.

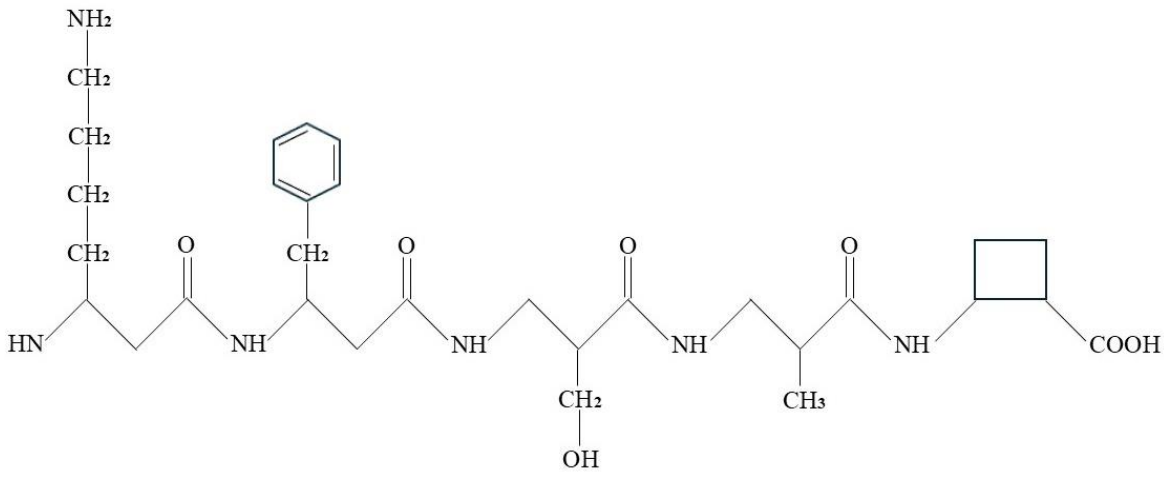
- The "K" in position 1 may be described as "N-(4-aminobutyl)glycine."
- The "F" in position 2 may be described as "N-(benzyl)glycine."
- The "X" in position 3 may be described as "N-(4-hydroxybutyl) glycine."
- The "X" in position 4 may be described as "N-(butyl) glycine."
- The "K" in position 5 may be described as "N-(4-aminobutyl)glycine."
- The "W" in position 6 may be described as "N-[1-(indol-3-yl)methyl]glycine."

CAUTION: The preferred representation of the sequences indicated above and their annotations is directed to the provision of a sequence listing on the filing date of a patent application. The same representation may not be applicable to a sequence listing provided subsequent to the filing date of a patent application, since consideration must be given to whether the information provided could be considered by an IPO to add subject matter to the original disclosure.

Relevant ST.26 paragraphs: Paragraphs 3(a), 3(e), 7(b), 29, 30

Example 29-5: Beta-amino acids

A patent application discloses the following sequence:



Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The sequence comprises beta-amino acids, which are encompassed by the definition of an "amino acid" as set forth in paragraph 3(a) of the Standard. A beta-amino acid has the amino group attached to the beta-carbon, the second carbon away from the carboxyl group. Paragraph 29 of the Standard requires representation of a modified amino acid that has a single carbon-containing side chain that is identical to the side chain in an L-alpha-amino acid listed in Annex I, Section 3, Table 3, which is located on any of the backbone atoms of an amino acid having an extended backbone, by the symbol of the corresponding unmodified amino acid.

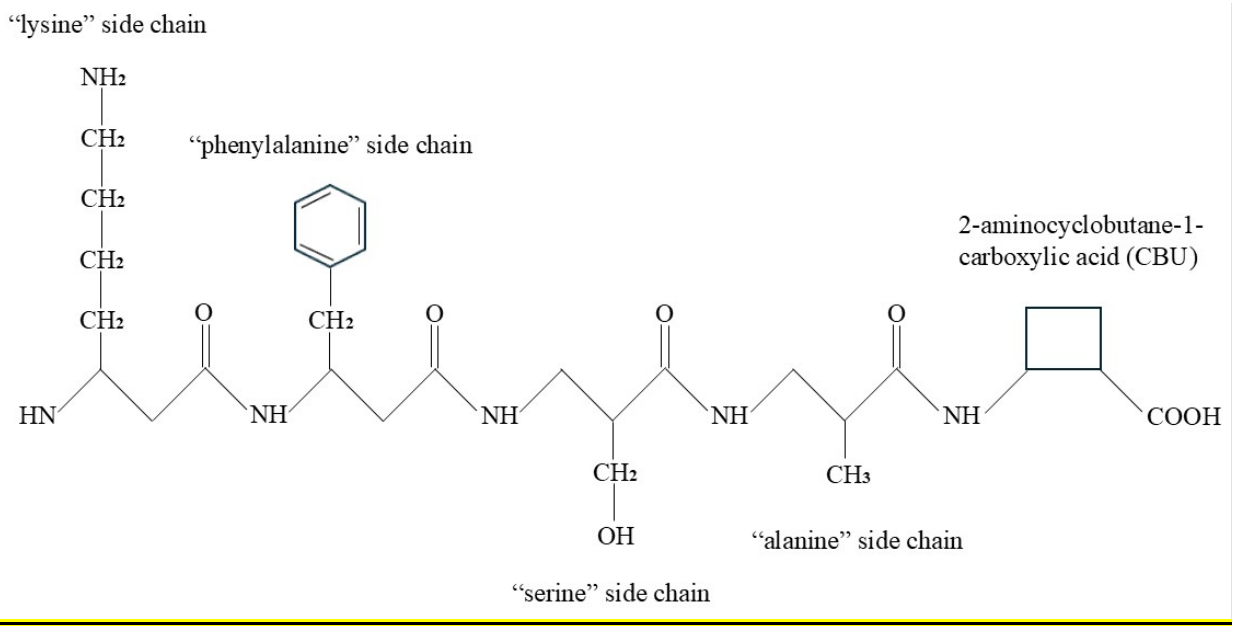
The first residue contains a single side chain attached to the extended backbone that is identical to the side chain of lysine.

The second residue contains a single side chain attached to the extended backbone that is identical to the side chain of phenylalanine.

The third residue contains a single side chain attached to the extended backbone that is identical to the side chain of serine.

The fourth residue contains a single side chain attached to the extended backbone that is identical to the side chain of alanine.

The fifth residue contains a cyclic side chain that is not identical to any ~~of the~~ side chain~~s~~ of ~~in~~ an L-alpha-amino acid listed in Annex I, Section 3, Table 3. Therefore, it may be represented by the symbol "X" or the most appropriate amino acid symbol.



Therefore, the disclosed peptide contains at least four modified amino acids that are specifically defined, and the sequence must be included in a sequence listing as required by ST.26 paragraph 7(b).

Question 3: How should the sequence(s) be represented in the sequence listing?

If "X" is deemed the most appropriate symbol for the fifth residue, the sequence must be included in a sequence listing as:

KFSAX (SEQ ID NO: 119)

Each residue must be described in a feature table using the feature key "SITE" and the mandatory qualifier "note" with a value that describes the residue by its chemical name.

- The "K" in position 1 may be described as "3,7-diaminoheptanoic acid."
- The "F" in position 2 may be described as "3-amino-4-phenylbutanoic acid."
- The "S" in position 3 may be described as "3-amino-2-(hydroxymethyl)propanoic acid."
- The "A" in position 4 may be described as "3-amino-2-methylpropanoic acid."
- The "X" in position 5 may be described as "2-aminocyclobutane-1-carboxylic acid."

CAUTION: The preferred representation of the sequences indicated above and their annotations is directed to the provision of a sequence listing on the filing date of a patent application. The same representation may not be applicable to a sequence listing provided subsequent to the filing date of a patent application, since consideration must be given to whether the information provided could be considered by an IPO to add subject matter to the original disclosure.

Relevant ST.26 paragraphs: Paragraphs 3(a), 3(e), 7(b), 27, 29, 30

Example 29-6: Peptide-peptoid hybrid

A patent application discloses the following:

"The antibacterial activity of the undecapeptide Lys-Lys-Leu-Leu-Lys-Leu-Leu-Lys-Leu-Leu-Leu was enhanced when 5 five positions were replaced with corresponding peptoid (i.e., N-substituted glycine) units, resulting in the peptide-peptoid hybrid sequence Lys-**Lys**-Leu-**Leu**-Lys-**Leu**-Leu-**Lys**-Leu-**Leu**-Leu. Bolded, underlined letters represent the corresponding peptoid unit."

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

Both the original peptide sequence Lys-Lys-Leu-Leu-Lys-Leu-Leu-Lys-Leu-Leu-Leu and the peptide-peptoid hybrid sequence Lys-**Lys**-Leu-**Leu**-Lys-**Leu**-Leu-**Lys**-Leu-**Leu**-Leu contain at least four specifically defined amino acids and must be included in a sequence listing as required by ST.26 paragraph 7(b).

Question 3: How should the sequence(s) be represented in the sequence listing?

The original peptide sequence must be included in a sequence listing as:

KKLLKLLKLLL (SEQ ID NO: 116)

The five "peptoid units" in the peptide-peptoid hybrid sequence are all N-substituted glycine residues and are encompassed by the definition of an "amino acid" as set forth in paragraph 3(a) of the Standard. Paragraph 29 requires representation of a modified amino acid that has a single carbon-containing side chain that is identical to the side chain in an L-alpha-amino acid listed in Annex I, Section 3, Table 3, which is located on the amino nitrogen of the residue, by the symbol of the corresponding unmodified amino acid. Therefore, each peptoid "Lys" must be represented in the sequence by "K" and each peptoid "Leu" must be represented in the sequence by "L." Accordingly, the peptide-peptoid hybrid sequence must be included in a sequence listing as:

KKLLKLLKLLL (SEQ ID NO: 117)

Each peptoid residue must each be described separately in a feature table using the feature key "SITE" and the mandatory qualifier "note" with a value that describes the residue by its chemical name.

- The peptoid "Lys" residues in positions 2 and 8 may be described as "N-(4-aminobutyl)glycine."
- The peptoid "Leu" residues in positions 4, 6, and 10 may be described as "N-(isobutyl)glycine."

Relevant ST.26 paragraphs: Paragraphs 3(a), 3(e), 7(b), 27, 29, 30

Paragraph 30 – Annotation of a modified amino acid

Example 30-1 – Feature key "CARBOHYD"

A patent application describes a polypeptide with a specifically modified amino acid, containing a glycosylated side chain, further characterized in that Cys corresponding to positions 4 and 15 of the polypeptide forms a disulfide bond, according to the following sequence:

Leu-Glu-Tyr-Cys-Leu-Lys-Arg-Trp-Asn(asialyloligosaccharide)-Glu-Thr-Ile-Ser-His-Cys-Ala-Trp

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The enumerated peptide ~~provides~~ contains 17 ~~specifically defined~~ amino acids. Since t~~T~~here are more than 4four specifically defined ~~16 natural~~ amino acids~~, wherein the ninth (asparagine) is glycosylated. Therefore~~, the sequence must be included in a sequence listing as required by ST.26 paragraph (7)(b).

Question 3: How should the sequence(s) be represented in the sequence listing?

The Asn in position 9 is modified by virtue of the asialyloligosaccharide attached to the side chain. According to ST.26 paragraph 29, a modified amino acid should be represented in the sequence as the corresponding unmodified amino acid whenever possible. Therefore, the Asn residue should be represented by "N".

~~Therefore~~ Accordingly, the sequence ~~must~~ should be included in a sequence listing as:

LEYCLKRWNETISHCAW (SEQ ID NO: 52)

~~A further description of the modified amino acid is required~~The modified amino acid must be further described in ~~the~~a feature table. The feature key "CARBOHYD" together with the ~~"~~mandatory~~"~~ qualifier "note" should be used to indicate the occurrence of the attachment of a sugar chain (asialyloligosaccharide) to ~~asparagine~~ Asn in position 9. The qualifier "note" must also describe~~s~~ the type of linkage, e.g.,
N-linked. The location descriptor in the feature location element is the residue position number of the modified ~~asparagine~~Asn.

In addition, there is a disulfide bond between the two Cys residues. Therefore, the feature key "DISULFID" should be used to describe an intrachain crosslink. The feature location element value is the residue position numbers of the linked Cys residues in "x..y" format, i.e., "4..15". The mandatory qualifier note should describe the intrachain disulfide bond.

Relevant ST.26 paragraph(s): 3(a), 7(b), 26, 29, **30**, 66(c), 70, and Annex I, section 7, feature key 7.4

Example 30-2 – Post-translationally modified amino acids

A patent application describes the following polypeptide:

Leu-Glu-Tyr-Cys-Leu-Lys-Arg-Trp-Glu-Thr-Ile-Ser-His

wherein the Arg at position 7 is post-translationally deiminated to citrulline.

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The enumerated peptide provides 13 specifically defined amino acids. Therefore, the sequence must be included in a sequence listing as required by ST.26 paragraph (7)(b).

Question 3: How should the sequence(s) be represented in the sequence listing?

According to ST.26 paragraph 29, a modified amino acid should be represented in the sequence as the corresponding unmodified amino acid whenever possible.

Therefore, the sequence should be included in a sequence listing as:

LEYCLKRWETISH (SEQ ID NO: 97)

where the symbol “R” is used to represent the arginine at position 7.

A further description indicating that the arginine at position 7 ~~may be~~is modified to citrulline is required. The modification of arginine to citrulline is a post-translational modification. Therefore, the feature key “MOD_RES” should be used together with the mandatory qualifier “note” to indicate that the arginine ~~may be~~is deiminated to form citrulline. The location descriptor in the feature location element is the residue position number of the modified arginine.

Relevant ST.26 paragraph(s): 3(a), 7(b), **30**, and Annex I, Section 7, Feature Key 7.18

Paragraph 36 – Sequences containing regions of an exact number of contiguous "n" or "X" residues

Example 36-1: Sequence with a region of a known number of "X" residues represented as a single sequence

LL-100-KYMR

Where the "-100-"between amino acids Leucine and Lysine reflects a 100 amino acid region in the sequence.

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

ST.26 paragraph 36 requires inclusion of a sequence that contains at least four specifically defined amino acids separated by one or more regions of a defined number of "X" residues.

The disclosed sequence uses a nonconventional symbol, i.e. "-100-." The definition of "-100-" must be determined from the explanation of the sequence in the disclosure, which defines this symbol as 100 amino acids between leucine and lysine (see Introduction to this document). Therefore, "-100-" is a defined region of "X" residues. Since six of the 106 amino acids in the sequence are specifically defined, ST.26 paragraph 7(b) requires that the sequence ~~must~~ be included in a sequence listing.

Question 3: How should the sequence(s) be represented in the sequence listing?

The nonconventional symbol "-100-" is represented as 100 "X" residues (since any symbol used to represent an amino acid is equivalent to only one residue). Therefore, a single sequence of 106 amino acids in length, containing 100 "X" residues between LL and KYMR, must be included in a sequence listing (SEQ ID NO: 53).

This sequence contains 100 "X" ~~variables~~ residues between LL and KYMR. The ST.26 default value for "X" with no further annotation, is any one of the unmodified L-alpha-amino acids "A", "R", "N", "D", "C", "Q", "E", "G", "H", "I", "L", "K", "M", "F", "P", "O", "S", "U", "T", "W", "Y", or "V" (paragraph 27). If these 100 "X" variables are defined as anything other than this default value, then a proper annotation for each "X" variable must be provided.

Relevant ST.26 paragraph(s): 7(b), 26, 27, and **36**

Example 36-2: Sequence with multiple regions of a known number or range of "X" residues represented as a single sequence

Lys-z_2-Lys-z_m-Lys-z_3-Lys-z_n-Lys-z_2-Lys

Where z is any amino acid, m=20, n=19-20, z_2 means that the ~~pairs of~~flanking ~~Lysines~~ lysines are separated by any two amino acids, and z_3 means the ~~pairs of~~flanking ~~Lysines~~ lysines are separated by any three amino acids.

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The disclosed sequence uses a nonconventional symbol, i.e. "z." Therefore, the disclosure must be consulted to determine the definition, and reveals that~~:~~ "z" is defined as any amino acid (see Introduction to this document). The conventional symbol used to represent any amino acid is "X". Considering the presence of "X" ~~variables~~residues, the peptide contains six lysine residues that are enumerated and specifically defined, which is required to be included in a sequence listing.

Question 3: How should the sequence(s) be represented in the sequence listing?

The sequence uses a nonconventional symbol "z", the definition of which must be determined from the disclosure. Since "z" is defined as any amino acid, the conventional symbol is "X."

The preferred and most encompassing means of representation is (see Introduction to this document):

KXXKXXXXXXXXXXXXXXXXXXXXKXXXKXXXXXXXXXXXXXXXXXXXXXXKXXK (SEQ ID NO: 54)

Wherein z_n is equal to 20 "X's", with a further description that the "X" ~~variable~~ residue corresponding to position 30 can be deleted.

Alternatively, or in addition to the above, the sequence may be represented as:

KXXKXXXXXXXXXXXXXXXXXXXXKXXXKXXXXXXXXXXXXXXXXXXXXXXKXXK (SEQ ID NO: 55)

Wherein z_n is equal to 19 "X's", with a further description that an "X" ~~variable~~ residue between position numbers 29 and 30 can be inserted.

According to paragraph 27, "X" will be construed as any one of the unmodified L-alpha-amino acids "A", "R", "N", "D", "C", "Q", "E", "G", "H", "I", "L", "K", "M", "F", "P", "O", "S", "U", "T", "W", "Y", or "V", except where it is used with a further description in the feature table. ~~Since~~ "X" in SEQ ID Nos 54 and 55 represents "any amino acid", which is broader in scope than the default value for "X" given in paragraph 27, since "any amino acid" encompasses modified or other amino acids. Therefore, each "X"~~:~~ must be annotated with the feature key VARIANT and a note qualifier with the value, "X can be any amino acid".

Where practicable, each "X" should be annotated individually. However, a region of contiguous "X" residues~~, or a multitude of "X" residues dispersed throughout the sequence,~~ may be jointly described with the feature key VARIANT using the syntax "x..y" as the location descriptor, where x and y are the positions of the first and last "X" residues, and a note qualifier with the value, "X can be any amino acid".

Relevant ST.26 paragraph(s): 26, 27, and **36**

Example 36-3: Sequence with multiple regions of a known number or range of "X" residues represented as a single sequence

K-z_2-K-z_m-K-z_3-K-z_n-K-z_2-K

Where z is any amino acid, where m=15-25, preferably 20-22, where n=15-25, preferably 19-20, where z_2 means that the pairs of flanking Lysines lysines are separated by any two amino acids, and z_3 means the pairs of flanking Lysines lysines are separated by any three amino acids.

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The sequence in the example uses a nonconventional symbol, i.e., "z." Therefore, the surrounding disclosure is consulted to determine the definition of "z" (see Introduction to this document). The disclosure defines this symbol as any amino acid. The conventional symbol used to represent a residue defined as "any amino acid" is "X." After considering the presence of "X" residues, the peptide contains 6 six lysine residues that are enumerated and specifically defined, which is required and must be included in a sequence listing.

Question 3: How should the sequence(s) be represented in the sequence listing?

The sequence uses a nonconventional symbol "z", the definition of which must be determined from the disclosure. Since "z" is defined as any amino acid, the conventional symbol is "X". The preferred and most encompassing means of representation is:

KXXKXXXXXXXXXXXXXXXXXXXXXXXXKXXXKXXXXXXXXXXXXXXXXXXXXXXXXXXXKXXK (SEQ ID NO: 56)

(where m=25 and n=25). The "z_m" region and the "z_n" region must each be annotated using the feature key VARIANT along with a mandatory "note" qualifier with a value indicating that , with a further description that up to 10 "X" residues in each of the "z_m" or "z_n" regions may be deleted.

Inclusion of any specific sequences essential to the disclosure or claims of the invention is strongly encouraged, as discussed in the introduction to this document.

Alternatively, the sequence may be represented as:

KXXKXXXXXXXXXXXXXXKXXXKXXXXXXXXXXXXXXXXKXXK (SEQ ID NO: 57)

(where m=15 and n=15). The "z_m" region and the "z_n" region must each be annotated using the feature key VARIANT along with a mandatory "note" qualifier with a value indicating that with a further description that up to 10 "X" residues in each of the "z_m" or "z_n" regions may be inserted.

As further alternatives, any or all possible variations may be included.

According to paragraph 27, "X" will be construed as any one of the unmodified L-alpha-amino acids "A", "R", "N", "D", "C", "Q", "E", "G", "H", "I", "L", "K", "M", "F", "P", "O", "S", "U", "T", "W", "Y", or "V", except where it is used with a further description in the feature table. Since "X" in SEQ ID Nos: 56 and 57 represents "any amino acid", which is broader in scope than the default value of "X" given in paragraph 27, since "any amino acid" encompasses modified or other amino acids. Therefore, each "X" it must be annotated with the feature key VARIANT and a note qualifier with the value, "X can be any amino acid".

Where practicable, each "X" should be annotated individually. However, a region of contiguous "X" residues, or a multitude of "X" residues dispersed throughout the sequence, may be jointly described with the feature key VARIANT using the syntax "x..y" as the location descriptor, where x and y are the positions of the first and last "X" residues, and a note qualifier with the value, "X can be any amino acid".

CAUTION: The preferred representation of the sequence indicated above is directed to the provision of a sequence listing on the filing date of a patent application. The same representation may not be applicable to a sequence listing provided subsequent to the filing date of a patent application, since consideration must be given to whether the information provided could be considered by an IPO to add subject matter to the original disclosure.

Relevant ST.26 paragraph(s): 27 and **36**

Paragraph 37 – Sequences containing regions of an unknown number of contiguous "n" or "X" residues

Example 37-1: Sequence with regions of an unknown number of "X" residues must not be represented as a single sequence I

Gly-Gly----Gly-Gly-Xaa-Xaa

where the symbol ---- is an undefined gap within the sequence, where Xaa is any amino acid, and where the ~~Glycine~~ glycine and Xaa residues are connected to one another through peptide bonds.

Question 1: Does ST.26 require inclusion of the sequence(s)?

NO

ST.26 paragraph 37 prohibits the inclusion of any sequence that contains an undefined gap; therefore, inclusion of the entire sequence is not required.

ST.26 paragraph 37 does require inclusion of any region of a sequence adjacent to an undefined gap that contains four or more specifically defined amino acids. In the example above, inclusion of either region adjacent to the undefined gap is not required, since each region contains only two specifically defined amino acids.

Question 2: Does ST.26 permit inclusion of the sequence(s)?

NO – not the entire sequence

~~**NO – not any region of the sequence**~~

ST.26 paragraph 37 does not permit inclusion of the entire sequence.

YES – each region adjacent to the undefined gap may be include in the sequence listing.

ST.26 paragraph 8 ~~does not permit~~permits inclusion of either region adjacent to the undefined gap, ~~since each~~which regions each contains only two specifically defined amino acids.

Question 3: How should the sequence(s) be represented in the sequence listing?

If included, ~~the following sequences should be included~~the regions adjacent to the undefined gap should be represented in the sequence listing as:

GG (SEQ ID NO: 120)

GGXX (SEQ ID NO: 121)

The two sequences should be annotated to indicate that they are part of a larger sequence that contains an undefind gap using the feature key "SITE" and the mandatory qualifier "note", wherein the value of the qualifier "note" indicates that the C-terminal residue of the GG sequence is linked to the N-terminal residue of the GGXX sequence by a gap of an undefined length.

Relevant ST.26 paragraphs: 7(b), 8, 26, and **37**

Example 37-2: Sequence with regions of an unknown number of "X" residues must not be represented as a single sequence II

Gly-Gly----Gly-Gly-Ala-Gly-Xaa-Xaa

wherein the symbol ---- is an undefined gap within the sequence, where Xaa is any amino acid, and the Gly~~cine~~ and Xaa residues are connected to one another through peptide bonds.

Question 1: Does ST.26 require inclusion of the sequence(s)?

NO – not the entire sequence

YES – ~~a region~~sa region of the sequence

ST.26 paragraph 37 prohibits the inclusion of any sequence that contains an undefined gap, but requires inclusion of any region of a sequence adjacent to an undefined gap that contains four or more specifically defined amino acids.

In the example above, ST.26 does not require (and prohibits) inclusion of ~~both~~ the entire sequence, which contains an undefined gap~~, and the Gly-Gly region adjacent to the undefined gap, which contains only two specifically defined amino acids.~~ However, ST.26 requires inclusion of the Gly-Gly-Ala-Gly- Xaa-Xaa region adjacent to the undefined gap, since it contains at least four specifically defined amino acids.

Question 2: Does ST.26 permit inclusion of the sequence(s)?

NO – not the entire sequence ~~and not the Gly-Gly region~~

YES – the Gly-Gly region may be included

ST.26 paragraph 37 does not permit the inclusion of the entire sequence.

ST.26 paragraph 8 permits the inclusion of sequences having fewer than four specifically defined amino acids.

Question 3: How should the sequence(s) be represented in the sequence listing?

The region of the sequence adjacent to the undefined gap that contains four specifically defined amino acids must be represented as:

GGAGXX (SEQ ID NO: 58)

The sequence should be annotated to indicate that the represented sequence is part of a larger sequence that contains an undefined gap by using the feature key "SITE", the feature location "1" and the qualifier "note" with the value, e.g., "This residue is linked N-terminally to a peptide ~~having~~ of undefined length that comprises an N-terminal Gly-Gly ~~and a gap of undefined length~~sequence".

According to paragraph 27, "X" will be construed as any one of the unmodified L-alpha-amino acids "A", "R", "N", "D", "C", "Q", "E", "G", "H", "I", "L", "K", "M", "F", "P", "O", "S", "U", "T", "W", "Y", or "V", except where it is used with a further description in the feature table. ~~Since~~ "X" in SEQ ID NO: 58 represents "any amino acid", which is broader in scope than the default value of "X" given in paragraph 27, since "any amino acid" encompasses modified or other amino acids. Therefore, each "X"~~it~~ must be annotated with the feature key VARIANT and a note qualifier with the value, "X can be any amino acid".

Where practicable, each "X" should be annotated individually. However, a region of contiguous "X" residues~~, or a multitude of "X" residues dispersed throughout the sequence,~~ may be jointly described with the feature key VARIANT using the syntax "x..y" as the location descriptor, where x and y are the positions of the first and last "X" residues, and a note qualifier with the value, "X can be any amino acid".

If included, the region of the sequence adjacent to the undefined gap that contains two specifically defined amino acids should be represented as:

GG (SEQ ID NO: 122)

The sequence should be annotated to indicate that the represented sequence is part of a larger sequence that contains an undefined gap by using the feature key "SITE", the feature location "2" and the qualifier "note" with the value "The peptide sequence C-terminal to this residue is undefined except for the terminal residues of GGAGXX."

Relevant ST.26 paragraph(s): 7(b), 8, 26, 27, and **37**

Paragraph 55 – A nucleotide sequence that contains both DNA and RNA segments

Example 55-1: Combined DNA/RNA ~~Molecule~~molecule

A patent application describes the following oligonucleotide sequence:

AGACCTTcggagucuccuguugaacagauagucaaaguagauC

Wherein the upper-case letters represent DNA residues and lower-case letters represent RNA residues.

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The disclosed sequence has more than ten enumerated and specifically defined nucleotides; therefore, it is required to be included in a sequence listing.

Question 3: How should the sequence(s) be represented in the sequence listing?

The nucleotide sequence must be included in a sequence listing as:

agaccttcggagtctcctgttgaacagatagtcaaagtagatc (SEQ ID NO: 93)

Note that the uracil nucleotides must be represented by the symbol “t” in the sequence listing.

ST.26 paragraph 55 dictates that a nucleotide sequence containing both DNA and RNA segments must be indicated as molecule type “DNA” and must be further described using the feature key “source” and both the mandatory qualifier “organism” with the value “synthetic construct” and the mandatory qualifier “mol_type” with the value “other DNA”. In addition, each segment of the sequence must be further described with the feature key “misc_feature,” and a feature location element with a value ~~which~~ that ~~includes~~ indicates the location of the segment, and the qualifier “note,” which indicates whether the segment is DNA or RNA. The disclosed sequence contains two DNA segments (nucleotide positions 1-7 and 43) and one RNA segment (nucleotide positions 8-42).

Relevant ST.26 paragraphs: 7, 14, **55**-56, and 83

Paragraph 89 – "CDS" ~~Feature~~ feature key

Example 89-1: Encoding nucleotide sequence and encoded amino acid sequence

A patent application describes the following nucleotide sequence and its translation:

```
atg acc gga aat aaa cct gaa acc gat gtt tac gaa att tta tga

Met Thr Gly Asn Lys Pro Glu Thr Asp Val Tyr Glu Ile Leu STOP
```

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The enumerated nucleotide sequence has more than ten specifically defined nucleotides.

The enumerated amino acid sequence has more than four specifically defined amino acids.

Question 3: How should the sequence(s) be represented in the sequence listing?

The nucleotide sequence must be presented as:

atgaccggaaataaacctgaaaccgatgtttacgaaattttatga (SEQ ID NO: 59)

The nucleotide sequence should further be described using the "CDS" feature key, and the element INSDFeature_location must identify the entire sequence, including the stop codon (i.e., position 1 through 45). In addition, the "translation" qualifier should be included with the qualifier value "MTGNKPETDVYEIL". The application does not disclose the genetic code table that applies to the translation (see Annex 1, Section 9, Table 7). If the Standard Code table applies, then the qualifier "transl_table" is not necessary; however, if a different genetic code table applies, then the appropriate qualifier value from Table 7 must be indicated for the qualifier "transl_table". Finally, the qualifier "protein_id" must be included with the qualifier value indicating the sequence identification number of the translated amino acid sequence.

The amino acid sequence must be separately presented with its own sequence identification number using single letter codes as follows:

MTGNKPETDVYEIL (SEQ ID NO: 60)

The STOP following the enumerated amino acid sequence must not be included in the amino acid sequence in the sequence listing.

CAUTION: The preferred representation of the sequence indicated above is directed to the provision of a sequence listing on the filing date of a patent application. The same representation may not be applicable to a sequence listing provided subsequent to the filing date of a patent application, since consideration must be given to whether the information provided could be considered by an IPO to add subject matter to the original disclosure.

Relevant ST.26 paragraphs: 7(a), 7(b), 26, 28, 89, 90, and 92

Example 89-2: Feature location extends beyond the disclosed sequence

A patent application contains the following figure disclosing a partial coding sequence and its translated amino acid sequence:

```
cat cac gca gca gaa tgt gga ttt tgt cct caa caa tgg caa gtt cta     48
His His Ala Ala Glu Cys Gly Phe Cys Pro Gln Gln Trp Gln Val Leu
1               5                   10                  15

cgt ggg agt ctg tgc att tgt gag ggt cca gct gaa gga tgg ttc ata     96
Arg Gly Ser Leu Cys Ile Cys Glu Gly Pro Ala Glu Gly Trp Phe Ile
            20                  25                  30

tca aga tgt tgg tta tgg tgt ggg cct caa gtc caa ggc ttt atc ttt    144
Ser Arg Cys Trp Leu Trp Cys Gly Pro Gln Val Gln Gly Phe Ile Phe
        35                  40                  45

gga gaa ggc aag gaa gga ggc ggt gac aga cgg gct gaa gcg agc cct    192
Gly Glu Gly Lys Glu Gly Gly Gly Asp Arg Arg Ala Glu Ala Ser Pro
    50                  55                  60

cag gag ttt tgg gaa tgc act tgg                                    216
Gln Glu Phe Trp Glu Cys Thr Trp
65                  70
```

Figure 1 – partial coding sequence of the *Homo sapi*ens *ITCH1* gene, which encodes amino acids 20 through 91 of the 442 amino acid long ITCH1 protein.

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The application discloses a nucleotide sequence and its translated amino acid sequence. The enumerated nucleotide sequence contains more than ten specifically defined nucleotides and must be included in a sequence listing.

The amino acid sequence contains more than four specifically defined amino acids and also must be included in a sequence listing as a separate sequence with its own sequence identification number.

Question 3: How should the sequence(s) be represented in the sequence listing?

The nucleotide sequence must be included in a sequence listing as:

catcacgcagcagaatgtggattttgtcctcaacaatggcaagttctacgtgggagtctgtgcatttgtgagggtccagctgaaggatggttcatatcaagatgttggt tatggtgtgggcctcaagtccaaggctttatctttggagaaggcaaggaaggaggcggtgacagacgggctgaagcgagccctcaggagttttgggaatgcact tgg (SEQ ID NO: 94)

The nucleotide sequence should further be described using a “CDS” feature key. The element INSDFeature_location must identify the location of the “CDS” feature in the sequence and must include the stop codon.

The figure describes a partial coding sequence that does not include the start codon or the stop codon. However, the description of the sequence indicates that the start codon is upstream of the nucleotide in position 1 and the stop codon is downstream of the last nucleotide in position 216.

ST.26 dictates that the location descriptor must not include numbering for residues beyond the range of the sequence in the INSDSeq_sequence element. Consequently, in the above example, the location descriptor for the CDS feature key cannot include position numbers outside the range of 1 through 216. The location of the stop codon in the element INSDFeature_location must be represented using the symbol “>” to indicate that the stop codon is located downstream of position 216. Likewise, the symbol “<” can be used to indicate that the location of the start codon is upstream of position 1. Thus, the location descriptor for the CDS feature key should appear as follows:

<1..>216

Note that “<” and “>” are reserved characters and will be replaced by “<” and “>”, respectively, in the XML instance of the sequence listing.

The “translation” qualifier should be included with the amino acid sequence of the protein as the qualifier value. The figure does not disclose the genetic code table that applies to the translation (see Annex 1, Section 9, Table 7). If the Standard Code table applies, then the qualifier “transl_table” is not necessary; however, if a different genetic code table applies, then the appropriate qualifier value from Table 7 of ST.26 Annex I must be indicated for the qualifier “transl_table”. Finally, the qualifier “protein_id” must be included in the CDS feature with the qualifier value indicating the sequence identification number of the translated amino acid sequence.

The translated amino acid sequence must be included as a separate sequence with its own sequence identification number:

HHAAECGFCPQQWQVLRGSLCICEGPAEGWFISRCWLWCGPQVQGFIFGEGKEGGGDRRAEASPQEFWECTW (SEQ ID NO: 95)

CAUTION: The preferred representation of the sequence indicated above is directed to the provision of a sequence listing on the filing date of a patent application. The same representation may not be applicable to a sequence listing provided subsequent to the filing date of a patent application, since consideration must be given to whether the information provided could be considered by an IPO to add subject matter to the original disclosure.

Relevant ST.26 paragraphs: 7, 41, 65, 66, 70, 71, 89, and 92

Paragraph 92 – Amino acid sequence encoded by a coding sequence

Example 92-1: Amino acid sequence encoded by a coding sequence with introns

A patent application contains the following figure disclosing a coding sequence and its translation:

```
atg aag act ttc gca gcc ttg ctt tcc gct gtc act ctc gcg ctc tcg
Met Lys Thr Phe Ala Ala Leu Leu Ser Ala Val Thr Leu Ala Leu Ser

gtg cgc gcc cag gcg gct gtc tgg agt caa t gtaagtgccg ctgcttttca
Val Arg Ala Gln Ala Ala Val Trp Ser Gln

ttgatacgag actctacgcc gagctgacgt gctaccgtat ag gt  ggc ggt aca
                                                Cys Gly Gly Thr

ccg ggt tgg acg ggc gag acc act tgc gtt gct ggt tcg gtt tgt acc
Pro Gly Trp Thr Gly Glu Thr Thr Cys Val Ala Gly Ser Val Cys Thr

tcc ttg agc tca gtgagcgact ttcaatccgt cgtcattgct cctcatgtat
Ser Leu Ser Ser

tgacgattgg ccttcatag tca tac tct caa tgc gtt ccg ggc tcc gca acg
                      Ser Tyr Ser Gln Cys Val Pro Gly Ser Ala Thr

tcc agc gct ccg gcg gcc ccc tca gcg aca act tca ggc ccc gca cct
Ser Ser Ala Pro Ala Ala Pro Ser Ala Thr Thr Ser Gly Pro Ala Pro

acg gac gga acg tgc tcg gcc agc ggg gca tgg ccg cca ttg acc tga
Thr Asp Gly Thr Cys Ser Ala Ser Gly Ala Trp Pro Pro Leu Thr Ter
```

Figure 1 – nucleotides shown in bold-face are intron regions.

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The application discloses a nucleotide sequence and its amino acid translation. The enumerated nucleotide sequence contains more than ten specifically defined nucleotides and must be included in a sequence listing as a single sequence.

The nucleotide sequence contains coding sequence (exons) separated by noncoding sequence (introns). The figure depicts the translation of the nucleotide sequence as three non-contiguous amino acid sequences. According to the figure caption, the bolded regions of nucleotides are intron sequences that will be spliced out of an RNA transcript before translation into a protein. Accordingly, the three amino acid sequences are actually a single, contiguous, enumerated sequence, which contains more than four specifically defined amino acids and must be included in a sequence listing as a single sequence.

Question 3: How should the sequence(s) be represented in the sequence listing?

The nucleotide sequence must be included in a sequence listing as:

atgaagactttcgcagccttgctttccgctgtcactctcgcgctctcggtgcgcgcccaggcggctgtctggagtcaatgtaagtgccgctgcttttcattgatacgaga
ctctacgccgagctgacgtgctaccgtataggtggcggtacaccgggttggacgggcgagaccacttgcgttgctggttcggtttgtacctccttgagctcagtgag
cgactttcaatccgtcgtcattgctcctcatgtattgacgattggccttcatagtcatactctcaatgcgttccgggctccgcaacgtccagcgctccggcggccccctc
agcgacaacttcaggccccgcacctacggacggaacgtgctcggccagcggggcatggccgccattgacctga (SEQ ID NO: 75)

The nucleotide sequence should further be described using a “CDS” feature key and the element INSDFeature_location must identify the location of the coding sequence, including the stop codon indicated by “Ter”. The CDS INSDFeature_location must use the “join” location operator to indicate that the translation products encoded by the indicated locations are joined and form a single, contiguous polypeptide using the format “join(x1..y1,x2..y2,x3..y3)”, e.g., “join(1..79,142..212,272..400)”. In addition, the “translation” qualifier should be included, with the amino acid sequence of the protein as the qualifier value. (Note that the terminator symbol “Ter” in the last position of the sequence must not be included in the amino acid sequence.) The application does not disclose the genetic code table that applies to the translation (see Annex 1, Section 9, Table 7). If the “Standard Code” table applies, then the qualifier “transl_table” is not necessary; however, if a different genetic code table applies, then the appropriate qualifier value from Table 7 must be indicated for the qualifier “transl_table”. Finally, the qualifier “protein_id” must be included with the qualifier value indicating the sequence identification number of the translated amino acid sequence. The amino acid sequence must be included as a single sequence:

MKTFAALLSAVTLALSVRAQAAVWSQCGGTPGWTGETTCVAGSVCTSLSSSYSQCVPGSATSSAPAAPSATTSG
PAPTDGTCSASGAWPPLT (SEQ ID NO: 76)

Relevant ST.26 paragraphs: 7, 26, 28, 57, 67, and 89-92

Paragraph 93 – Primary sequence and a variant, each enumerated by its residues

Example 93-1: Representation of enumerated variants I

The description includes the following sequence alignment.

```
D. melanogaster      ACATTGAATCTCATACCACTTT
D. virilis           ...-..G...C..--.G.....
D. simulans          GT..G.CG..GT..SGT.G...
```

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

It is common in the art to include “dots” in a sequence alignment to indicate “this position is the same as the position above it.” Therefore, the “dots” in *D.virilis* and *D. simulans* sequences are considered enumerated and specifically defined nucleotides, as they are simply a short-hand way of indicating that a given position is the same nucleotide as in *D. melanogaster*. In addition, sequence alignments frequently display the symbol “-“ to indicate the absence of a residue in order to maximize the alignment.

Accordingly, the nucleotide sequences of *D. melanogaster* and *D. simulans* contain twenty-two enumerated and specifically defined nucleotides, whereas the nucleotide sequence of *D. virilis* contains nineteen. Thus, each sequence is required by ST.26 paragraph 7(a) to be included in a sequence listing with separate sequence identification numbers.

Question 3: How should the sequence(s) be represented in the sequence listing?

Drosophila melanogaster sequence must be included in a sequence listing as:

acattgaatctcataccacttt (SEQ ID NO: 61)

Drosophila virilis sequence must be included in a sequence listing as:

acatggatcccacgacttt (SEQ ID NO: 62)

Drosophila simulans sequence must be included in a sequence listing as:

gtatggcgtcgtatsgtagttt (SEQ ID NO: 63)

Relevant ST.26 paragraphs: 7(a), 13, and 93

Example 93-2: Representation of enumerated variants II

The description includes the following table of a peptide and functional variants thereof. A blank space in the table below indicates that an amino acid in the variant is the same as the corresponding amino acid in the “Sequence” and a “-“ indicates deletion of the corresponding amino acid in the “Sequence”.

Position	1	2	3	4	5	6	7	8	9
Sequence	A	V	L	T	Y	L	R	G	E
Variant 1									A
Variant 2			P			P			
Variant 3			A	I	G	Y			
Variant 4							-		

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

As indicated, a blank space in this table indicates that an amino acid in the variant is the same as the corresponding amino acid in the “Sequence”. Therefore, the amino acids of the variant sequences are enumerated and specifically defined.

Since the four variant sequences each contain more than four enumerated and specifically defined amino acids, each sequence is required by ST.26 paragraph 7(b) to be included in a sequence listing with separate sequence identification numbers.

Question 3: How should the sequence(s) be represented in the sequence listing?

AVLTYLRGE (SEQ ID NO: 77)

AVLTYLRGA (SEQ ID NO: 78)

AVPTYPRGE (SEQ ID NO: 79)

AVAIGYRGE (SEQ ID NO: 80)

AVLTYLGE (SEQ ID NO: 81)

Relevant ST.26 paragraphs: 7(b), 26, and 93

Example 93-3: Representation of a consensus sequence

A patent application includes Figure 1 with the following multiple sequence alignment.

Consensus	LEG**n**EQFINA**ak**IIRHP**k**Y**nrk**T**ln**NDI**m**LIK
Homo sapiens	LEG**N**EQFINA**AK**IIRHP**Q**Y**DRK**T**LN**NDI**M**LIK
Pongo abelii	LEG**N**EQFINA**AK**IIRHP**Q**Y**DRK**T**VN**NDI**M**LIK
Papio Anubis	LEG**T**EQFINA**AK**IIRHP**D**Y**DRK**T**LN**NDI**L**LIK
Rhinopithecus roxellana	LEG**T**EQFINA**AK**IIRHP**N**Y**NRI**T**LD**NDI**L**LIK
Pan paniscus	LEG**N**EQFINA**AK**IIRHP**K**Y**NRI**T**LN**NDI**M**LIK
Rhinopithecus bieti	LEG**N**EQFINA**TK**IIRHP**K**Y**NGN**T**LN**NDI**M**LIK
Rhinopithecus roxellana	LEG**N**EQFINA**TQ**IIRHP**K**Y**NGN**T**LN**NDI**M**LIK

The consensus sequence includes ~~upper~~ upper-case letters to represent conserved amino acid residues, while the ~~lower~~ lower-~~case~~

letters “n”, “a”, “k”, “r”, “l” and “m” represent the predominant amino acid residues among the aligned sequences.

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The ~~lower case~~lower-case letters in the consensus sequence each represent a single amino acid residue. Consequently, the consensus sequence, as well as each of the remaining seven sequences in Figure 1, includes at least four specifically defined amino acids. ST.26 paragraph 7(b) requires inclusion of all eight sequences in the sequence listing.

Question 3: How should the sequence(s) be represented in the sequence listing?

The ~~lower case~~lower-case letters in the consensus sequence are being used as ambiguity symbols to represent the predominant amino acid among the possible variants for a specific position. Therefore, the ~~lower case~~lower-case letters “n”, “a”, “k”, “r”, “l” and “m” are conventional symbols used in a nonconventional manner and the consensus sequence must be represented using an ambiguity symbol in place of each of the ~~lower case~~lower-case letters.

The most restrictive ambiguity symbol should be used. For most positions in the consensus sequence, “X” is the most restrictive ambiguity symbol; however, the most restrictive ambiguity symbol for “D” or “N” in positions 20 and 25 is “B”. The consensus sequence should be included in the sequence listing as:

LEGXEQFINAXXIIRHPXYBXXTXBNDIXLIK (SEQ ID NO: 82)

According to paragraph 27, the symbol “X” will be construed as any one of the unmodified L-~~l~~alpha amino acids “A”, “R”, “N”, “D”, “C”, “Q”, “E”, “G”, “H”, “I”, “L”, “K”, “M”, “F”, “P”, “O”, “S”, “U”, “T”, “W”, “Y”, or “V”, except where it is used with a further description in the feature table. Therefore, each “X” in the consensus sequence must be further described in a feature table using the feature key “VARIANT” and the qualifier “note” to indicate the possible variants for each position.

The remaining seven sequences must be included in the sequence listing as:

LEGNEQFINAAKIIRHPQYDRKTLNNDIMLIK (SEQ ID NO: 83)

LEGNEQFINAAKIIRHPQYDRKTVNNDIMLIK (SEQ ID NO: 84)

LEGTEQFINAAKIIRHPDYDRKTLNNDILLIK (SEQ ID NO: 85)

LEGTEQFINAAKIIRHPNYNRITLDNDILLIK (SEQ ID NO: 86)

LEGNEQFINAAKIIRHPKYNRITLNNDIMLIK (SEQ ID NO: 87)

LEGNEQFINATKIIRHPKYNGNTLNNDIMLIK (SEQ ID NO: 88)

LEGNEQFINATQIIRHPKYNGNTLNNDIMLIK (SEQ ID NO: 89)

CAUTION: The preferred representation of the sequence indicated above is directed to the provision of a sequence listing on the filing date of a patent application. The same representation may not be applicable to a sequence listing provided subsequent to the filing date of a patent application, since consideration must be given to whether the information provided could be considered by an IPO to add subject matter to the original disclosure.

Relevant ST.26 paragraphs: 7(b), 26, 27, 93, and 97

Paragraph 94 – Variant sequence disclosed as a single sequence with enumerated alternative residues

Example 94-1: Representation of single sequence with enumerated alternative amino acids

A patent application claims a peptide of the sequence:

(i) Gly-Gly-Gly-[Leu or Ile]-Ala-Thr-[Ser or Thr]

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The sequence provides ~~four~~ five specifically defined amino acids and ST.26 paragraph 7(b) requires inclusion of the sequence in a sequence listing.

Question 3: How should the sequence(s) be represented in the sequence listing?

Table 3 of Annex I, Section 3 defines the ambiguity symbol “J” as isoleucine or leucine. Therefore, the preferred representation of the sequence is:

GGGJATX (SEQ ID NO: 64)

which requires a further description in a feature table using the feature key “VARIANT” and the qualifier “note” to indicate that the “X” is serine or threonine.

Alternatively, the sequence may be represented, for example, as:

GGGLATS (SEQ ID NO: 65)

which requires a further description in a feature table using the feature key “VARIANT” and the qualifier “note” to indicate that L can be replaced by I, and S can be replaced by T.

CAUTION: The preferred representation of the sequence indicated above is directed to the provision of a sequence listing on the filing date of a patent application. The same representation may not be applicable to a sequence listing provided subsequent to the filing date of a patent application, since consideration must be given to whether the information provided could be considered by an IPO to add subject matter to the original disclosure.

Relevant ST.26 paragraph(s): 7(b), ~~8,~~ 26, 27, 94, and 97

Example 94-2 – Representation of single sequence with enumerated alternative amino acids that may be modified amino acids

A patent application describes the following polypeptide:

Leu-Glu-Tyr-Cys-Leu-Lys-Arg-Trp-Xaa-Glu-Thr-Ile-Ser-His-Cys-Ala-Trp

where Xaa can be Ile, Ala, Phe, Tyr, alle, Melle, or Nle.

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The enumerated peptide provides 16 specifically defined amino acids. Therefore, the sequence must be included in a sequence listing as required by ST.26 paragraph (7)(b).

Question 3: How should the sequence(s) be represented in the sequence listing?

The most restrictive ambiguity symbol that can encompass “Ile, Ala, Phe, Tyr, alle, Melle, or Nle” is “X”. Therefore, the sequence must be included in a sequence listing as:

LEYCLKRWXETISHCAW (SEQ ID NO: 96)

The alternative amino acid residues encompassed by “X” at postion 9 include modified amino acids (i.e., alle, Melle and Nle). ST.26 paragraph 30 requires that “[a] modified amino acid must be further described in the feature table”. However, paragraph 30 does not require any specific feature key be used to describe modified amino acids. While paragraph 30 describes the use of feature keys “CARBOHYD”, “LIPID”, “MOD_RES”, and “SITE”, these feature keys are more appropriate for scenarios where the modified amino acid is not within a list of alternatives for a specific location. In this example, the feature key “VARIANT” satisfies the requirement of paragraph 30 since it allows for the inclusion of all of the alternatives for the variant site. So, the feature key “VARIANT” with the qualifier “note” and “Ile, Ala, Phe, Tyr, alle, Melle, or Nle” as a qualifier value should be used to describe the variant site at position 9. The use of a second feature key such as “SITE” with a qualifier “note” may be used to further identify ~~the~~ each alternative modified amino acid~~s~~ found at position 9.

Relevant ST.26 paragraph(s): 3(a), 7(b), 27, 30, **94**, 96, and Annex I, Section 4, Table 4

Paragraph 95(a) – A variant sequence disclosed only by reference to a primary sequence with multiple independent variations

Example 95(a)-1: Representation of a variant sequence by annotation of the primary sequence

An application contains the following disclosure:

"Peptide fragment 1 is Gly-Leu-Pro-Xaa-Arg-Ile-Cys wherein Xaa can be any amino acid….

In another embodiment, peptide fragment 1 is Gly-Leu-Pro-Xaa-Arg-Ile-Cys wherein Xaa can be Val, Thr, or Asp….

In another embodiment, peptide fragment 1 is Gly-Leu-Pro-Xaa-Arg-Ile-Cys wherein Xaa can be Val."

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

"Peptide fragment 1" in each of the three disclosed embodiments provides at least six specifically defined amino acids; therefore, the sequence must be included in a sequence listing as required by ST.26 paragraph 7(b).

Question 3: How should the sequence(s) be represented in the sequence listing?

In this example, the enumerated sequence of "Peptide fragment 1" is disclosed three times, as three different embodiments, each with an alternative description of Xaa. In this example, "X" is the most restrictive ambiguity symbol for the Xaa position.

ST.26 requires inclusion of the disclosed enumerated sequence only once. In the most encompassing of the three embodiments, Xaa is any amino acid (see Introduction to this document). Therefore, the sequence that must be included in the sequence listing is:

GLPXRIC (SEQ ID NO: 66)

According to paragraph 27, "X" will be construed as any one of the unmodified L-alpha-amino acids "A", "R", "N", "D", "C", "Q", "E", "G", "H", "I", "L", "K", "M", "F", "P", "O", "S", "U", "T", "W", "Y", or "V", except where it is used with a further description in the feature table. ~~Since~~ "X" in SEQ ID NO: 66 represents "any amino acid", which is broader in scope than the default value of "X" given in paragraph 27, since "any amino acid" encompasses modified or other amino acids. Therefore, it must be annotated with the feature key VARIANT and a note qualifier with the value, "X can be any amino acid".

~~Where practicable, each "X" should be annotated individually. However, a region of contiguous "X" residues, or a multitude of "X" residues dispersed throughout the sequence, may be jointly described with the feature key VARIANT using the syntax "x..y" as the location descriptor, where x and y are the positions of the first and last "X" residues, and a note qualifier with the value, "X can be any amino acid".~~

Inclusion of any additional sequences essential to the disclosure or claims of the invention is strongly encouraged, as discussed in the introduction to this document.

For the above example, it is strongly encouraged that the following additional three sequences are included in the sequence listing, each with their own sequence identification number:

GLPVRIC (SEQ ID NO: 67)

GLPTRIC (SEQ ID NO: 68)

GLPDRIC (SEQ ID NO: 69)

CAUTION: The preferred representation of the sequence indicated above is directed to the provision of a sequence listing on the filing date of a patent application. The same representation may not be applicable to a sequence listing provided subsequent to the filing date of a patent application, since consideration must be given to whether the information provided could be considered by an IPO to add subject matter to the original disclosure.

Relevant ST.26 paragraph(s): 7(b), 26, 27, and **95(a)**

Paragraph 95(b) – A variant sequence disclosed only by reference to a primary sequence with multiple interdependent variations

Example 95(b)-1: Representation of individual variant sequences with multiple interdependent variations

A patent application describes the following consensus sequence:

cgaatg**n**$_1$cccactacgaatg**n**$_2$cacgaatg**n**$_3$cccaca

wherein n_1, n_2, and n_3 can be a, t, g, or c.

Several variant sequences are disclosed as follows:

if n_1 is a, then n2 and n3 are t, g, or c;

if n_1 is t, then n2 and n3 are a, g, or c;

if n_1 is g, then n2 and n3 are t, a, or c;

if n_1 is c, then n2 and n3 are t, g, or a.

Question 1: Does ST.26 require inclusion of the sequence(s)?

YES

The sequence has more than ten enumerated and "specifically defined" nucleotides and is required by ST.26 paragraph 7(a) to be included in a sequence listing.

Question 3: How should the sequence(s) be represented in the sequence listing?

The enumerated sequence contains more than ten specifically defined nucleotides and three "n" residues. ST.26 requires inclusion of the disclosed enumerated sequence and where an ambiguity symbol is appropriate, the most restrictive symbol should be used. In this example, n_1, n_2, and n_3 can be a, t, g, or c, so "n" is the most restrictive ambiguity symbol. Therefore, the sequence that must be included in the sequence listing is:

cgaatgncccactacgaatgncacgaatgncccaca (SEQ ID NO: 70)

ST.26 paragraph 15 states that "the symbol "n" will be construed as any one of unmodified "a", "c", "g", or "t/u" except where it is used with a further description in the feature table. Since the value of every "n" residue in this sequence is equivalent to the default "a", "c", "g", or "t", no further annotation is required.

The enumerated sequence contains variations at three distinct locations and the occurrence of the variations is interdependent. Inclusion of additional sequences which represent additional embodiments that are a key part of the invention is **strongly** encouraged, as discussed in the ~~introduction~~ Introduction to this document. Therefore, according to ST.26 paragraph 95(b), the following additional embodiments should be included in a sequence listing as four separate sequences, each with its own sequence identification number:

cgaatgacccactacgaatgbcacgaatgbcccaca (SEQ ID NO: 71)

cgaatgtcccactacgaatgvcacgaatgvcccaca (SEQ ID NO: 72)

cgaatggcccactacgaatghcacgaatghcccaca (SEQ ID NO: 73)

cgaatgccccactacgaatgdcacgaatgdcccaca (SEQ ID NO: 74)

(Note that b = t, g, or c; v = a, g, or c; h = t, a, or c; and d = t, g, or a; see Annex I, Section 1, Table 1)

According to ST.26 paragraph 15, the most restrictive symbol must be used to represent variable positions. Consequently, n2 and n3 must not be represented by "n" in the sequences.

CAUTION: The preferred representation of the sequence indicated above is directed to the provision of a sequence listing on the filing date of a patent application. The same representation may not be applicable to a sequence listing provided subsequent to the filing date of a patent application, since consideration must be given to whether the information provided could be considered by an IPO to add subject matter to the original disclosure.

Relevant ST.26 paragraphs: 7(a), 15, and 95(b)

[Appendix to Annex VI follows]

APPENDIX

GUIDANCE DOCUMENT SEQUENCES IN XML

The Appendix is available at:
https://www.wipo.int/standards/en/xml_material/st26/st26-annex-vi-appendix-guidance-document-sequences_v2_0~~1_7~~.xml

[Annex VII follows]

ANNEX VII

RECOMMENDATION FOR THE TRANSFORMATION OF A SEQUENCE LISTING FROM ST.25 TO ST.26: POTENTIAL ADDED OR DELETED SUBJECT MATTER

Version ~~1.7~~ 2.0

Revision approved by the Committee on WIPO Standards (CWS)
at its ~~eleventh~~ thirteenth session on ~~December 8, 2023~~ November 14, 2025

Introduction

The requirements for the presentation of nucleotide and amino acid sequences differ between WIPO Standards ST.25 and ST.26. Consequently, the question has been raised as to whether Standard ST.26 would require addition or deletion of any subject matter in a sequence listing submitted as part of an international application under Standard ST.26 that may not be supported by an application from which priority is claimed.

Scope of the Document

This document addresses the mandatory requirements of ST.26, and any potential consequences of those requirements. This document does not address every possible scenario; if the means of representation in ST.26, of information contained in an ST.25 sequence listing, is not clear, then the information may always be included in the application description to avoid deleted subject matter.

Recommendations for Potential Added or Deleted Subject Matter

Review of the issues contained in this document demonstrates that transformation from ST.25 to ST.26 by itself should not inherently result in added or deleted subject matter, in particular, where the ST.25 sequence listing was fully compliant with Standard ST.25. However, there are certain scenarios that will require applicant caution. Recommendations have been provided to avoid added or deleted subject matter.

Scenario 1

ST.25 uses numeric identifiers to tag various types of data, e.g., <110> for Applicant Name. ST.26 uses terms in the English language, as element names and attributes, for data tagging.

Recommendation:

The ST.26 terms simply describe the type of data content; therefore, the use of the ST.26 element names and attributes does not constitute added subject matter.

Scenario 2

ST.26 explicitly requires inclusion of: (a) branched sequences; (b) sequences with D-amino acids; (c) nucleotide analogues; and (d) sequences with abasic sites. Under ST.25, the requirement for inclusion or the prohibition of such sequences is not clear.

Recommendation:

The disclosure contained in the application should be sufficient to represent these sequences in an ST.26 sequence listing, when they may not have been included in an ST.25 sequence listing. For certain types of information required by ST.26, care must be taken not to add subject matter beyond that disclosed, e.g., see discussion below (in Scenario 4) on the mol_type qualifier for nucleotide sequences.

Scenario 3

ST.26 ~~excludes~~ permits the inclusion of sequences with less than 10 specifically defined nucleotides (not including “n”) and less than 4 specifically defined amino acids (not including “X”).

Recommendation:

~~The excluded sequences may be included in the application body, where those sequences have not already been included therein.~~ Sequences with less than 10 specifically defined nucleotides and less than 4 specifically defined amino acids may remain in the ST.26 sequence listing. Alternatively, these sequences may be removed from the sequence listing. If the latter option is chosen, care should be taken that the removed sequences are included in the application body, if those sequences have not yet been defined there.

Scenario 4

For both nucleotide sequences and amino acid sequences, ST.26 has the mandatory feature key "source" with two mandatory qualifiers, one of which is 'mol_type'. ST.25 has a corresponding feature key for nucleotide sequences (which is rarely used) with no corresponding qualifiers and there is no corresponding feature key for amino acid sequences.

Nucleotide sequences
ST.26 - feature key 5.37 source; mandatory qualifier 6.39 mol_type (see ST.26 paragraph 75)

Qualifier	Value
mol_type	genomic DNA
	genomic RNA
	mRNA
	tRNA
	rRNA
	other DNA (applies to synthetic molecules)
	other RNA (applies to synthetic molecules)
	transcribed RNA
	viral cRNA
	unassigned DNA (applies where *in vivo* molecule is unknown)
	unassigned RNA (applies where *in vivo* molecule is unknown)

Amino acid sequences
ST.26 - feature key 7.30 source; mandatory qualifier 8.1 mol_type (see ST.26 paragraph 75)

Qualifier	Value
mol_type	protein

Recommendation:

The only issue of concern is the controlled vocabulary values associated with the mol_type qualifier for nucleotide sequences. Some of the value choices listed above may not be sufficiently supported in the disclosure. Added subject matter may be avoided, however, by use of the most generic value for a particular sequence, e.g., "other DNA" and "other RNA" for a synthetic molecule and "unassigned DNA" and "unassigned RNA" for an *in vivo* molecule.

Scenario 5

Where a sequence includes "Xaa", ST.25 requires that further information concerning that residue be included in field <223>, which accompanies fields <221> (feature name) and <222> (feature location). ST.25 does not provide a default value for "Xaa" ("X" in ST.26). However, ST.26 does provide such a default value, and therefore, further information is not always required. Two of the most frequently used annotations in peptide sequences is "any amino acid" or "any naturally occurring amino acid" for variable "Xaa" or "X". This language could be interpreted to include amino acids other than those listed in the amino acid tables contained in either ST.25 or ST.26. The ST.26 default value for "X" with no further annotation, is any of the 22 individual amino acids listed in Annex I (see Section 3, Table 3). This ST.26 default value may itself constitute added or deleted subject matter, and therefore, adversely affect the scope of a patent application when transitioning from ST.25 to ST.26.

Recommendations:

(a) Where the ST.25 sequence listing includes a <221> feature name, <222> feature location corresponding to the Xaa, and <223> further information on Xaa, and the <221> feature name is also an appropriate ST.26 feature key, e.g., SITE, VARIANT, or UNSURE, then the ST.26 feature key should be used. Furthermore, to avoid potential deleted subject matter, the information in field <223> must be included in an accompanying qualifier "note".

(b) Where the ST.25 sequence listing includes a <221> feature name, <222> feature location corresponding to the Xaa, and <223> further information on Xaa, and the <221> feature name is not an ST.26 feature key, then ST.26 feature keys SITE or REGION, as appropriate, should be used. Furthermore, to avoid potential deleted subject matter, the information in field <223>, as well as the inappropriate <221> feature name, must be included in an accompanying qualifier "note". For example, an ST.25 listing used a feature name that is not in ST.25 or ST.26, <221> Variable, together with further information <223> Xaa is any amino acid. In this example, the value of the ST.26 qualifier note would be "Variable – Xaa is any amino acid".

(c) Where the ST.25 sequence listing provides no <221>, <222>, or <223> field corresponding to the Xaa or where fields <221> and <222> corresponding to the Xaa are included, but no information is included in a corresponding <223> field (neither scenario is compliant with ST.25, but has occurred nonetheless), any information contained in the application body to describe "Xaa" should be included in the ST.26 qualifier "note" together with an appropriate feature key, e.g., SITE, REGION, or UNSURE, and location.

Scenario 6

In ST.25, uracil is represented in the sequence by "u" and thymine is represented by "t". In ST.26, uracil and thymine are both represented in the sequence by "t" and without further annotation; "t" represents uracil in RNA and thymine in DNA.

Recommendations:

(a) Where a DNA sequence contains uracil, ST.26 considers it to be a modified nucleotide, and requires that uracil must be represented as a "t" and be further described using the feature key "modified_base", the qualifier "mod_base" with "OTHER" as the qualifier value and the qualifier "note" with "uracil" as the qualifier value. This ST.26 annotation is not considered added subject matter where the ST.25 DNA sequence contained a "u".

(b) Where an RNA sequence contains thymine, ST.26 considers it to be a modified nucleotide, and requires that thymine must be represented as a "t" and be further described using the feature key "modified_base", the qualifier "mod_base" with "OTHER" as the qualifier value and the qualifier "note" with "thymine" as the qualifier value. This ST.26 annotation is not considered added subject matter where the ST.25 RNA sequence contained a "t".

Scenario 7

In both ST.25 and ST.26, modified nucleotides or amino acids must have a further description. In ST.26, the identity of a modified nucleotide may be indicated using an abbreviation from Annex I, Section 2, Table 2, where applicable. Otherwise, the complete unabbreviated name of the modified nucleotide must be indicated. Similarly, the identity of a modified amino acid may be indicated using an abbreviation from Annex I, Section 4, Table 4, where applicable. Otherwise, the complete unabbreviated name of the modified amino acid must be indicated. In contrast, if a modified residue is not contained in an ST.25 table, use of the complete, unabbreviated name is not required, and not infrequently, an abbreviation is used instead.

Recommendations:

(a) Where only an abbreviated name, which is not in Annex I, Section 2, Table 2 or Section 4, Table 4, was used both in the application and in an ST.25 sequence listing for either a modified nucleotide or a modified amino acid, and the abbreviated name is known in the art to reference only one specific modified nucleotide or modified amino acid, then use of the full, unabbreviated name would not itself constitute added subject matter.

(b) Where only an abbreviated name, which is not in Annex I, Section 2, Table 2 or Section 4, Table 4, was used both in the application and in an ST.25 sequence listing for either a modified nucleotide or a modified amino acid (and the application contains no chemical structure), and the abbreviated name is not known in the art to reference one specific modified nucleotide or modified amino acid, i.e., the abbreviation is either not known at all in the art, or could possibly represent multiple different modified nucleotides or modified amino acids, then compliance with ST.26, without introduction of added subject matter, is not possible in this situation. Of course in this case, the priority application and sequence listing are themselves vague. To avoid potential deleted subject matter, the abbreviated name from the ST.25 sequence listing should be placed in an ST.26 "note" qualifier in addition to the value of the complete unabbreviated name of the modified nucleotide or modified amino acid. The complete unabbreviated name of the modified nucleotide or modified amino acid required in an ST.26 sequence listing will not be afforded priority to the earlier application. Care should be taken to draft the original (ST.25) sequence listing and application disclosure to include the unabbreviated name to avoid future issues.

Scenario 8

ST.25 contains a number of feature keys that are not contained in ST.26. Therefore, applicants must take care to capture the information contained in those ST.25 feature keys in a manner compliant with ST.26 without the introduction of added or deleted subject matter.

Recommendations:

The following table provides guidance as to the manner in which the information contained in a former ST.25 feature key may be included in compliance with ST.26 without the introduction of added or deleted subject matter. Numbers 1-23 are feature keys related to nucleotide sequences and numbers 24–43 are feature keys related to amino acid sequences.

No.	ST.25 Feature key <221>	ST.26 equivalent		
		Feature key	Qualifier	Qualifier value
1	allele	misc_feature	allele	<223> value
2	attenuator	regulatory[1]	regulatory_class[1]	"attenuator"
			note *(if <223> present)*	<223> value
3	CAAT_signal	regulatory[1]	regulatory_class[1]	"CAAT_signal"
			note *(if <223> present)*	<223> value
4	conflict	misc_feature	note	"conflict" and <223> value
5	enhancer	regulatory[1]	regulatory_class[1]	"enhancer"
			note *(if <223> present)*	<223> value
6	GC_signal	regulatory[1]	regulatory_class[1]	"GC_signal"
			note *(if <223> present)*	<223> value
7	LTR	mobile_element[1]	rpt_type[1]	"long_terminal_repeat"
			note *(if <223> present)*	<223> value
8	misc_signal	regulatory[1]	regulatory_class[1]	"other"
			note *(if <223> present)*	<223> value
9	mutation	variation	note	"mutation" and <223> value
10	old_sequence	misc_feature	note	"old_sequence" and <223> value
11	polyA_signal	regulatory[1]	regulatory_class[1]	"polyA_signal_sequence"
			note *(if <223> present)*	<223> value
12	promoter	regulatory[1]	regulatory_class[1]	"promoter"
			note *(if <223> present)*	<223> value
13	RBS	regulatory[1]	regulatory_class[1]	"ribosome_binding_site"
			note *(if <223> present)*	<223> value
14	repeat_unit (a) when repeat_region not used	misc_feature	note	"repeat_unit" and <223> value
	repeat_unit (b) when repeat_region used	repeat_region	rpt_unit_range	1st residue..last residue
			note *(if <223> present)*	<223> value
15	satellite	repeat_region	satellite	"satellite" (or "microsatellite" or "minisatellite" – if supported)
			note *(if <223> present)*	<223> value
16	scRNA	ncRNA[1]	ncRNA_class[1]	"scRNA"
			note *(if <223> present)*	<223> value
17	snRNA	ncRNA[1]	ncRNA_class[1]	"snRNA"
			note *(if <223> present)*	<223> value
18	TATA_signal	regulatory[1]	regulatory_class[1]	"TATA_box"[2]
			note	TATA_signal and (if <223> present): <223> value
19	terminator	regulatory[1]	regulatory_class[1]	"terminator"
			note *(if <223> present)*	<223> value
20	3'clip	misc_feature	note	"3'clip" and <223> value
21	5'clip	misc_feature	note	"5'clip" and <223> value
22	-10_signal	regulatory[1]	regulatory_class[1]	"minus_10_signal"
			note *(if <223> present)*	<223> value
23	-35_signal	regulatory[1]	regulatory_class[1]	"minus_35_signal"
			note *(if <223> present)*	<223> value

[1] ST.26 may require that a specific ST.25 feature, e.g., TATA_signal, be replaced by a broader feature key/qualifier/value, e.g., regulatory/regulatory_class/TATA_box. .

[2] In order to avoid addition of subject-matter that may lead to partial loss of priority, it is recommended to include the more limited term "TATA_signal" in a "note" qualifier as shown in the above table (item N° 18). If in rare cases the Applicant considers that the use of the "TATA_box" value for the "regulatory_class" qualifier is not appropriate, the value:"other" may be used instead of "TATA_box". In this case, the term "TATA_signal" must be included in a "note" qualifier associated to the "regulatory" feature key.

No.	ST.25 Feature key <221>	ST.26 equivalent		
		Feature key	Qualifier	Qualifier value
24	NON_CONS	This feature relates to a gap of an unknown number of residues in a single sequence, which is prohibited in both ST.25 (paragraph 22) and ST.26 (paragraph 37). Consequently, each region of specifically defined residues that is encompassed by ST.26 paragraph 7 must be included in the sequence listing as a separate sequence and assigned its own sequence identification number. To avoid added/deleted subject matter, each such sequence must be annotated to indicate that it is part of a larger sequence that contains an undefined gap.		
		REGION	note	Description
		Description - as to where and to what the sequence is linked, e.g., this residue is linked N-terminally to a peptide having an N-terminal Gly-Gly and a gap of undefined length.		
25	SIMILAR	REGION	note	"SIMILAR" and <223> value if present
26	THIOETH	CROSSLNK	note	"THIOETH" and <223> value if present
		For further location information guidance, see ST.26 Annex I, CROSSLNK Feature Key Comment		
27	THIOLEST	CROSSLNK	note	"THIOLEST" and <223> value if present
		For further location information guidance, see ST.26 Annex I, CROSSLNK Feature Key Comment		
28	VARSPLIC	Discussed in a Scenario 13 below		
29	ACETYLATION	MOD_RES	note	"ACETYLATION" and <223> value if present
			note	Information required by ST.26 Annex I MOD_RES Feature Key Comment, if possible (without added subject matter)
30	AMIDATION	MOD_RES	note	"AMIDATION" and <223> value if present
			note	Information required by ST.26 Annex I MOD_RES Feature Key Comment, if possible (without added subject matter)
31	BLOCKED	MOD_RES	note	"BLOCKED" and <223> value if present
			note	Information required by ST.26 Annex I MOD_RES Feature Key Comment, if possible (without added subject matter)
32	FORMYLATION	MOD_RES	note	"FORMYLATION" and <223> value if present
			note	Information required by ST.26 Annex I MOD_RES Feature Key Comment, if possible (without added subject matter)
33	GAMMA-CARBOXYGLUTAMIC ACID HYDROXYLATION	MOD_RES	note	"GAMMA-CARBOXYLGLUTAMIC ACID HYDROXYLATION" and <223> value if present
			note	Information required by ST.26 Annex I MOD_RES Feature Key Comment, if possible (without added subject matter)
34	METHYLATION	MOD_RES	note	"METHYLATION" and <223> value if present
			note	Information required by ST.26 Annex I MOD_RES Feature Key Comment, if possible (without added subject matter)
35	PHOSPHORYLATION	MOD_RES	note	"PHOSPHORYLATION" and <223> value if present
			note	Information required by ST.26 Annex I MOD_RES Feature Key Comment, if possible (without added subject matter)
36	PYRROLIDONE CARBOXYLIC ACID	MOD_RES	note	"PYRROLIDONE CARBOXYLIC ACID" and <223> value if present
			note	Information required by ST.26 Annex I MOD_RES Feature Key Comment, if possible (without added subject matter)

No.	ST.25 Feature key <221>	ST.26 equivalent		
		Feature key	Qualifier	Qualifier value
37	SULFATATION	MOD_RES	note	"SULFATATION" and <223> value if present
			note	Information required by ST.26 Annex I MOD_RES Feature Key Comment, if possible (without added subject matter)
38	MYRISTATE	LIPID	note	"MYRISTATE" and <223> value if present
			note	Information required by ST.26 Annex I LIPID Feature Key Comment, if possible (without added subject matter)
39	PALMITATE	LIPID	note	"PALMITATE" and <223> value if present
			note	Information required by ST.26 Annex I LIPID Feature Key Comment, if possible (without added subject matter)
40	FARNESYL	LIPID	note	"FARNESYL" and <223> value if present
			note	Information required by ST.26 Annex I LIPID Feature Key Comment, if possible (without added subject matter)
41	GERANYL-GERANYL	LIPID	note	"GERANYL-GERANYL" and <223> value if present
			note	Information required by ST.26 Annex I LIPID Feature Key Comment, if possible (without added subject matter)
42	GPI-ANCHOR	LIPID	note	"GPI-ANCHOR" and <223> value if present
			note	Information required by ST.26 Annex I LIPID Feature Key Comment, if possible (without added subject matter)
43	N-ACYL DIGLYCERIDE	LIPID	note	"N-ACYL DIGLYCERIDE" and <223> value if present
			note	Information required by ST.26 Annex I LIPID Feature Key Comment, if possible (without added subject matter)

Scenario 9

Certain feature keys present in both ST.25 and in ST.26, both for nucleotide sequences and amino acid sequences, have mandatory qualifiers in ST.26, as indicated below. The nucleotide sequence feature key "modified_base" is also present in both ST.25 and ST.26; however, Scenario 7 contains appropriate recommendations. ST.25 did not have any qualifiers, but did have a <223> free text field. When the information contained in an ST.25 <223> field is appropriate as the value for the ST.26 mandatory qualifier, then the information should be included as such. When an ST.25 <223> field has either not been provided or contains information that is not appropriate as the value for the ST.26 mandatory qualifier, then applicants must take care to capture the information contained in the ST.25 feature key/<223> field in a manner compliant with ST.26 without the introduction of added or deleted subject matter.

Nucleotide sequences[3]

Feature Key	Mandatory Qualifier
5.12 - misc_binding	6.3 - bound_moiety
5.30 - protein_bind	6.3 - bound_moiety

[3] The numeric references in the table below refer to the Feature key and Qualifier numbers of ST.26, Annex I Controlled Vocabulary.

Recommendations:

(a) If the ST.25 <223> field is absent or inappropriate, and the application description disclosed the name of the molecule/complex that may bind to the feature location of the nucleic acid, then that name should be included in the qualifier “bound_moiety”.

(i) Any information contained in the ST.25 <223> field that is inappropriate for inclusion in the qualifier “bound_moiety” should be inserted into an appropriate optional qualifier of the feature key, e.g., “note”.

(b) If the ST.25 <223> field is absent or inappropriate, and the application description did not disclose the name of the molecule/complex that may bind to the feature location of the nucleic acid, then the ST.26 feature key “misc_feature” should be used instead of misc_binding or protein_bind, with the qualifier “note”.

(i) If the ST.25 <223> field was absent, then the value of the qualifier “note” should be the name of the ST.25 feature key;

(ii) If the ST.25 <223> field contained inappropriate information, then the value of the qualifier “note” should be the name of the ST.25 feature key and the information from the <223> field.

Amino acid sequences[4]

Feature Key	Mandatory Qualifier
7.2 – BINDING	8.2 – note
7.4 – CARBOHYD	8.2 – note
7.10 – DISULFID	8.2 – note
7.11 – DNA_BIND	8.2 – note
7.12 – DOMAIN	8.2 – note
7.16 – LIPID	8.2 – note
7.17 – METAL	8.2 – note
7.18 – MOD_RES	8.2 – note
7.23 – NP_BIND	8.2 – note
7.29 – SITE	8.2 – note
7.39 – ZN_FING	8.2 – note

Recommendations:

(a) If the ST.25 <223> field is absent or inappropriate, and the application description disclosed the specific information required in the mandatory qualifier, then that information should be included in the mandatory qualifier “note”.

(i) Any information contained in the ST.25 <223> field that is inappropriate for inclusion in the mandatory qualifier “note” (see feature key definition and comment) should be inserted into a second qualifier “note”.

(b) If the ST.25 <223> field is absent or inappropriate, and the application description did not disclose the specific information required in the mandatory qualifier, then the ST.26 feature key “SITE” (for one amino acid) or “REGION” (for a range of amino acids) should be used instead, with the qualifier “note”.

(i) If the ST.25 <223> field is absent, then the value of the qualifier “note” should be the name of the ST.25 feature key;

(ii) If the ST.25 <223> field contained inappropriate information, then the value of the qualifier “note” should be the name of the ST.25 feature key and the information from the <223> field.

Scenario 10

Each specific feature key in ST.25 has a <222> field to indicate a feature location; however, ST.25 does not require an indication of the location for most features and the format of the location information is not standardized. Furthermore, ST.25 does not have location operators, e.g., “join”. ST.26 has standardized location descriptors and operators and each feature must contain at least one location descriptor. (CDS features are a special case and are discussed below in Scenario 11).

[4] The numeric references in the table below refer to the Feature key and Qualifier numbers of ST.26, Annex I Controlled Vocabulary.

Recommendations:

(a) If the ST.25 sequence listing had a <222> field, direct importation or importation into ST.26 format should not raise any added subject matter consideration;

(b) If the ST.25 sequence listing did not have a <222> field, but location information was contained in the application description, then direct importation or importation into ST.26 format should not raise any added subject matter consideration;

(c) If neither the ST.25 sequence listing, nor the application description contained location information, then presumably, the feature applies to the entire sequence. (Indicating a location that is less than the entire sequence without support in the application description would likely constitute added/deleted subject matter.) Care should be taken to draft the original (ST.25) sequence listing and application disclosure to include location information to the extent possible to avoid future issues.

Scenario 11

In ST.25, a coding sequence that encoded a single, contiguous polypeptide but that was interrupted by one or more non-coding sequence(s), e.g., introns, was indicated as multiple separate CDS features, as illustrated below:

<220>
<221> CDS
<222> (1)..(571)

<220>
<221> CDS
<222> (639)..(859)

In contrast, ST.26 has a join location operator that specifies that the polypeptides encoded by the indicated locations are joined and form a single, contiguous polypeptide. (Note: both ST.25 and ST.26 require that the stop codon be included in the CDS feature location.)

Recommendations:

(a) If the ST.25 sequence listing or the application description clearly indicated that the polypeptide sequences encoded by the multiple separate CDS features form a single, contiguous polypeptide, then a coding sequence interrupted by an intron in a single CDS feature must be represented with the join location operator, as illustrated below, such that no added subject matter is introduced:

<INSDFeature_key>CDS</INSDFeature_key>
<INSDFeature_location>join(1..571,639..859)</INSDFeature_location>

(b) If the ST.25 sequence listing or the application description did not indicate that the polypeptide sequences encoded by the two separate CDS features form a single, contiguous polypeptide, then use of the join location operator would likely constitute added subject matter.

Scenario 12

ST.25 specifies that feature names must be one from Table 5 or 6. However, U.S. regulations indicated that these feature names were recommended, but not required. Therefore, a sequence in an ST.25 sequence listing (compliant with U.S. regulations) might have a “custom” feature key name with no corresponding feature key in ST.26. It is also possible that no feature name was provided for the <221> field or the <221> field is absent. These scenarios may be handled in a similar manner.

Recommendation:

The “custom” feature key name from ST.25 may be represented in an ST.26 sequence listing with no added subject matter as follows:

Type	ST.25 Feature Key <221>	Potential ST.26 Equivalent		
		Feature key	Qualifier	Qualifier value
NA	“Custom” feature key	misc_feature	note	“custom” feature key name and <223> value if present
AA	“Custom” feature key	SITE or REGION	note	“custom” feature key name and <223> value if present

Scenario 13

ST.25 contains a feature key “VARSPLIC” defined as “description of sequence variants produced by alternative splicing”. In ST.26, “VARSPLIC” has been replaced with the broader feature key VAR_SEQ defined as “description of sequence variants produced by alternative splicing, alternative promoter usage, alternative initiation and ribosomal frameshifting”. Therefore, the ST.26 sequence listing should not use “VAR_SEQ” as a replacement of “VARSPLIC” without a further explanation.

Recommendation:

In ST.26 the feature “VAR_SEQ” should be used with the qualifier “note”, whose value should include an explanation of the ST.25 narrower scope, e.g., “sequence variant produced by alternative splicing”. Any additional information contained in an accompanying ST.25 <223> field should also be included in the qualifier “note”.

Scenario 14

If the source of a sequence was artificial, the ST.25 <213> Organism field requires the phrase “Artificial Sequence”. In ST.26, the feature key “source” requires the qualifier “organism”, whose value must be indicated as “synthetic construct”, rather than “Artificial Sequence”.

Recommendation:

The value for the ST.26 qualifier “organism” must be indicated as “synthetic construct”. To avoid potential deleted subject matter, any explanatory information contained in the required ST.25 <223> field should be included in a qualifier “note” (of the feature key “source”).

Scenario 15

If the scientific name of the source organism of a sequence is unknown, the ST.25 <213> Organism field requires the term “Unknown”. In ST.26, the feature key “source” requires the qualifier “organism”, whose value must be indicated as “unidentified”, rather than “Unknown”.

Recommendation:

The value for the ST.26 qualifier “organism” must be indicated as “unidentified”. To avoid potential deleted subject matter, any explanatory information contained in the required ST.25 <223> field should be included in a qualifier “note” (of the feature key “source”).

Scenario 16

ST.25 allows for the enumeration of amino acids to optionally include negative numbers, counting backwards starting with the amino acid next to number 1, for the amino acids preceding the mature protein, for example pre-sequences, pro-sequences, pre-pro-sequences and signal sequences. ST.26 does not allow for negative numbers in the feature location.

Recommendations:

(a) If the ST.25 sequence listing had a feature or features represented in a <221> and an accompanying <222> field which contained negative and/or positive numbering, e.g., “PROPEP” and/or “CHAIN”, then in the ST.26 sequence listing, the appropriate feature key, e.g., “PROPEP” and/or “CHAIN”, should be used. A qualifier “note” may be used with the information in a <223> field, if any, as the qualifier value;

(b) If the ST.25 sequence listing did not have a feature or features represented in a <221> and accompanying <222> field, but information was contained in the application description regarding the negative and/or positive numbering, then in the ST.26 sequence listing, the appropriate feature key, e.g., “PROPEP” and/or “CHAIN”, should be used. Otherwise, the feature key “REGION” may be used. A qualifier “note” may be used with information in the application description, if any, as the qualifier value;

(c) If neither the ST.25 sequence listing, nor the application description, contains information explaining the negative and/or positive numbering, then to avoid potential deleted subject matter in the ST.26 sequence listing, the “REGION” feature key should be used, where the feature location spans the negatively numbered region of the ST.25 sequence. Also, a qualifier “note” should be used to indicate that the amino acid sequence was negatively numbered in the ST.25 sequence listing of the application to which priority is claimed.

Scenario 17

ST.25 provides for publication information in fields <300> to <313>. ST.26 does not provide for inclusion of such information.

Recommendation:

The information contained in ST.25 fields <300> to <313> should be inserted into the accompanying application body, if not already contained therein.

Scenario 18

ST.25 does not provide a standardized way to indicate that a CDS region of a nucleotide sequence was to be translated using a genetic code table other than the standard genetic code table. In contrast, ST.26 has a "transl_table" qualifier that can be used with the "CDS" feature key to indicate that the region is to be translated using an alternative genetic code table. If the "transl_table" qualifier is not used, the use of the standard genetic code table is assumed.

Recommendations:

(a) If the ST.25 sequence listing or the application description clearly indicated that a CDS region is to be translated using an alternative genetic code table, then the "transl_table" qualifier must be used with the appropriate genetic code table number as the qualifier value. Failure to use the "transl_table" qualifier would likely constitute added subject matter, as the default "Standard Code" table would be assumed. Failure to include, in the ST.26 sequence listing, the alternative genetic code table information from the ST.25 sequence listing or from the application description would likely constitute deleted subject matter.

(b) If the ST.25 sequence listing or the application description did not indicate that a CDS region is to be translated using an alternative genetic code table, then the "transl_table" qualifier should not be used, or should be used only with the qualifier value "1," i.e., the Standard Code table. Use of the "transl_table" qualifier with any qualifier value other than "1" would likely constitute added and deleted subject matter.

Scenario 19

ST.25 does not provide a standardized way to indicate the location of a feature, in particular, one contained in a site or region that extends beyond a specified residue or span of residues, e.g., a CDS region of a nucleotide sequence that extends beyond one or both ends of a disclosed sequence. In contrast, the ST.26 feature location descriptor provides a standardized way to indicate the location of such a site or region by using the "<" or ">" symbols. For example, the "CDS" feature location must include the stop codon, even when the stop codon is not included in the disclosed sequence itself, by indicating the location as e.g., 1..>321.

Recommendations:

(a) Where the ST.25 sequence listing did not explicitly indicate that the location of a feature extended beyond the sequence, but such a location is either supported by the disclosure or is clear from the sequence itself, e.g., the stop codon of a CDS feature that is not contained in the sequence, then the "<" or ">" symbols may be used in the ST.26 sequence listing without addition of subject matter.

(b) Where the ST.25 sequence listing did not explicitly indicate that the location of a feature extended beyond the sequence, and such a location is neither supported by the disclosure, nor is clear from the sequence itself, then compliance with ST.26, without introduction of added subject matter, may not be possible in this situation. In this case, the priority application and sequence listing are themselves arguably incomplete. In this situation, the location description of the feature in the ST.26 sequence listing will not be afforded priority to the earlier application. Care should be taken to draft the original (ST.25) sequence listing and application disclosure to include complete feature information.

Scenario 20

ST.25 Appendix I requires that where a nucleotide sequence contains both DNA and RNA fragments, the value in <212> shall be "DNA" and the combined DNA/RNA molecule shall be further described in the <220> to <223> feature section; however, the exact nature of the further description is not clear and this requirement is not routinely followed. ST.26, paragraph 55, requires that each
DNA and RNA segment (ST.26 uses "segment" rather than "fragment" for internal consistency) of the combined DNA/RNA molecule must be further described with the feature key "misc_feature", which includes the location of the segment, and the qualifier "note", which indicates whether the segment is DNA or RNA.

Recommendations:

(a) If the ST.25 sequence listing described the DNA and RNA segments in one or more features using <221> misc_feature, appropriate locations in <222>, and indications in <223> as to which segments were DNA or RNA, then incorporating that information into ST.26 format, using a misc_feature for each DNA and RNA segment, should not raise any added subject matter consideration;

(b) If the ST.25 sequence listing described the DNA and RNA segments in one or more features using a feature key in <221> other than misc_feature, appropriate locations in <222>, and indications in <223> identifying which segments are DNA or RNA, then incorporating that information into ST.26 format, using a misc_feature for each DNA and RNA segment and an additional "note" qualifier with the original <221> feature key as the value, should not raise any added or deleted subject matter consideration;

(c) If the ST.25 sequence listing provides the identity (DNA or RNA) and location of each segment in a <223> field that is not associated with a <221> and <222> field, e.g., the explanation for an Artificial Sequence, then incorporating that information into ST.26 format using a misc_feature for each DNA and RNA segment, should not raise any added subject matter consideration;

(d) If the ST.25 sequence listing described the molecule in a feature using a <221> misc_feature and a <223> noting that the molecule is a combined DNA/RNA molecule, but did not provide location information for each segment, and

(i) If the description provided the locations of each DNA and RNA segment, then incorporating that information into ST.26 format using a misc_feature for each DNA and RNA segment, should not raise any added subject matter consideration;

(ii) If the description does not contain the location information of each DNA and RNA segment, then compliance with ST.26, without introduction of added subject matter, may not be possible in this situation. In this case, the priority application and sequence listing are themselves arguably incomplete. In this situation, any location descriptions of the features in the ST.26 sequence listing will not be afforded priority to the earlier application. Care should be taken to draft the original (ST.25) sequence listing and application disclosure to include complete feature information.

(e) If the ST.25 sequence listing described the molecule in a feature using a feature key in <221> other than misc_feature and a <223> noting that the molecule is a combined DNA/RNA molecule, but did not provide location information for each segment, and

(i) If the description provided the locations of each DNA and RNA segment, then incorporating that information into ST.26 format using a misc_feature for each DNA and RNA segment and an additional “note” qualifier with the original <221> feature key as the value, should not raise any added or deleted subject matter consideration;

(ii) If the description does not contain the location information of each DNA and RNA segment, then compliance with ST.26, without introduction of added subject matter, may not be possible in this situation. In this case, the priority application and sequence listing are themselves arguably incomplete. In this situation, any location descriptions of the features in the ST.26 sequence listing will not be afforded priority to the earlier application. Care should be taken to draft the original (ST.25) sequence listing and application disclosure to include complete feature information.

(f) If the ST.25 sequence listing noted that the molecule is a combined DNA/RNA molecule in a <223> field, e.g., the explanation for an Artificial Sequence, but did not provide any feature key or location information of each segment, and

(i) If the description provided the locations of each DNA and RNA segment, then incorporating that information into ST.26 format using a misc_feature for each DNA and RNA segment, should not raise any added subject matter consideration;

(ii) If the description does not contain the location information of each DNA and RNA segment, then compliance with ST.26, without introduction of added subject matter, may not be possible in this situation. In this case, the priority application and sequence listing are themselves arguably incomplete. In this situation, any location descriptions of the features in the ST.26 sequence listing will not be afforded priority to the earlier application. Care should be taken to draft the original (ST.25) sequence listing and application disclosure to include complete feature information.

[End of Annex VII and of Standard]