STANDARD ST.26

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

Version 1.3

Approved by the Committee on WIPO Standards (CWS) at its seventh session on July 5, 2019

Editorial Note prepared by the International Bureau

At its fifth session, the Committee on WIPO Standards (CWS) agreed that the transition from WIPO Standard ST.25 to Standard ST.26 takes place in January 2022. Meanwhile, Standard ST.25 should continue to be used.

The Standard is published for information purposes of industrial property offices and other interested parties.
TABLE OF CONTENTS

INTRODUCTION ........................................................................................................................................................... 3
DEFINITIONS ............................................................................................................................................................... 3
SCOPE .......................................................................................................................................................................... 4
REFERENCES .............................................................................................................................................................. 5
REPRESENTATION OF SEQUENCES ......................................................................................................................... 5
   Nucleotide sequences ........................................................................................................................................... 5
   Amino acid sequences ........................................................................................................................................... 8
   Presentation of special situations ........................................................................................................................ 9
STRUCTURE OF THE SEQUENCE LISTING IN XML .................................................................................................. 9
   Root element ............................................................................................................................................................ 10
   General information part ....................................................................................................................................... 10
   Sequence data part ............................................................................................................................................... 14
   Feature table .......................................................................................................................................................... 15
   Feature keys .......................................................................................................................................................... 16
   Mandatory feature keys ....................................................................................................................................... 16
   Feature location .................................................................................................................................................... 16
   Feature qualifiers .................................................................................................................................................. 18
   Mandatory feature qualifiers ............................................................................................................................ 18
   Qualifier elements ............................................................................................................................................... 18
   Free text ............................................................................................................................................................... 20
   Coding sequences .................................................................................................................................................. 20
   Variants ............................................................................................................................................................... 21

ANNEXES
Annex I  -  Controlled vocabulary
Annex II  -  Document Type Definition for Sequence Listing (DTD)
Annex III  -  Sequence Listing Specimen (XML file)
Annex IV  -  Character Subset from the Unicode Basic Latin Code Table for Use in an XML Instance of a Sequence Listing
Annex V  -  Additional data exchange requirements (for patent offices only)
Annex VI  -  Guidance document
   Appendix - Guidance document sequences in XML
Annex VII - Recommendation for the transformation of a sequence listing from ST.25 to ST.26:
   potential added or deleted subject matter
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 industrial 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 any amino acid that can be represented using any of the symbols set forth in Annex I (see Section 3, Table 3). 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-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 HisHisHisHisHisGln); or

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

(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 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-pyrolysine, 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 3’-monophosphate, deoxyguanosine 3’-monophosphate, deoxycytidine 3’-monophosphate, deoxymethidine 3’-monophosphate, adenosine 3’-monophosphate, guanosine 3’-monophosphate, cytidine 3’-monophosphate, or uridine 3’-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 nucleotide analogues 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.

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 bonds.

8. A sequence listing must not 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/


   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 the Gregorian Calendar;

   WIPO Standard ST.3 Two-Letter Codes for the Representation of States, Other Entities and Intergovernmental Organizations;

   WIPO Standard ST.16 Identification of different kinds of patent documents;

   WIPO Standard ST.25 Presentation of nucleotide and amino acid sequence listings.

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'-end to 3'-end direction from left to right, or in the direction from left to right that mimics the 5'-end to 3'-end 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 direction 5' to 3', or in the direction that mimics the direction 5' to 3'. 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 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 "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 92 to 98.

16. Modified nucleotides should be represented in the sequence as the corresponding unmodified nucleotides, i.e., "a", "c", "g" or "t" whenever possible. 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". Where the symbol "n" is used to represent a modified nucleotide it 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 95 and 96). 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 "xanthine" 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>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>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 "a", "c", "g", "t", or "n" residues for which the same description applies may be jointly described using a single INSDFeature element with the location descriptor in the element INSDFeature_location (see paragraphs 64 to 71). For representation of sequence variants, i.e., deletions, insertions or substitutions, see paragraphs 92 to 98.

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>
    <INSDQualifier>
      <INSDQualifier_name>isoguanine</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 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 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 “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”, together with a further description in the feature table, e.g., as provided by paragraphs 29, 30, 32, or 92-96. For representation of sequence variants, i.e., alternatives, deletions, insertions, or substitutions, see paragraphs 92 to 98.

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 the corresponding unmodified amino acids whenever possible. 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”. 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 qualifier “NOTE”. The feature key “MOD_RES” should be used for other post-translationally modified amino acids together with the qualifier “NOTE”; otherwise the feature key “SITE” together with the 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

```xml
<INSDFeature>
  <INSDFeature_key>MOD_RES</INSDFeature_key>
  <INSDFeature_location>3</INSDFeature_location>
  <INSDFeature_quals>
    <INSDFeature_key>NOTE</INSDFeature_key>
    <INSDFeature_value>3Hyp</INSDFeature_value>
  </INSDFeature_quals>
</INSDFeature>
```

Example 2: Non post-translationally modified amino acid

```xml
<INSDFeature>
  <INSDFeature_key>SITE</INSDFeature_key>
  <INSDFeature_location>3</INSDFeature_location>
  <INSDFeature_quals>
  </INSDFeature>
```

Date: September 2019
Example 3: D-amino acid

```
<INSDFeature>
  <INSDFeature_key>SITE</INSDFeature_key>
  <INSDFeature_location>9</INSDFeature_location>
  <INSDQualifier>
    <INSDQualifier_name>NOTE</INSDQualifier_name>
    <INSDQualifier_value>D-Arginine</INSDQualifier_value>
  </INSDQualifier>
</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>
  <INSDQualifier>
    <INSDQualifier_name>NOTE</INSDQualifier_name>
    <INSDQualifier_value>A or V</INSDQualifier_value>
  </INSDQualifier>
</INSDFeature>
```

34. A region containing a known number of contiguous “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 70). For representation of sequence variants, i.e., deletions, insertions, or substitutions, see paragraphs 92 to 98.

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

   (b) 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 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 1.2//EN"
        "ST26SequenceListing_V1_2.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, may be composed of any Unicode characters except the reserved characters, which must be replaced as set forth in paragraph 41; and

   (b) the information contained in all other elements of the general information part and in all elements of the sequence data part must be composed of printable characters (including the space character) from the Unicode Basic Latin code table excluding the reserved characters, which must be replaced as set forth in paragraph 41, (i.e., limited to Unicode code points 0020, 0021, 0023 through 0026, 0028 through 003B, 003D, and 003F through 007E – see Annex IV), and the only character entities permitted are the predefined entities set forth in paragraph 41.

41. In an XML instance of a sequence listing, 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:

<table>
<thead>
<tr>
<th>Reserved Character</th>
<th>Predefined Entities</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;</td>
<td>&lt;</td>
</tr>
<tr>
<td>&gt;</td>
<td>&gt;</td>
</tr>
<tr>
<td>&amp;</td>
<td>&amp;</td>
</tr>
<tr>
<td>'</td>
<td>&quot;</td>
</tr>
<tr>
<td>'</td>
<td>'</td>
</tr>
</tbody>
</table>

See paragraph 71 for an example.

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 not appear in the XML instance (except as provided for in paragraph 95 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:

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Description</th>
<th>Mandatory/Optional</th>
</tr>
</thead>
<tbody>
<tr>
<td>dtdVersion</td>
<td>Version of the DTD used to create this file in the format &quot;V#_#&quot;, e.g., &quot;V1_2&quot;.</td>
<td>Mandatory</td>
</tr>
<tr>
<td>fileName</td>
<td>Name of the sequence listing file.</td>
<td>Optional</td>
</tr>
<tr>
<td>softwareName</td>
<td>Name of the software that generated this file.</td>
<td>Optional</td>
</tr>
<tr>
<td>softwareVersion</td>
<td>Version of the software that generated this file.</td>
<td>Optional</td>
</tr>
<tr>
<td>productionDate</td>
<td>Date of production of the sequence listing file (format &quot;CCYY-MM-DD&quot;).</td>
<td>Optional</td>
</tr>
</tbody>
</table>

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

        <ST26SequenceListing dtdVersion="V1_2" fileName="US11_405455_SEQL.xml"
        softwareName="SEQL-software-name" softwareVersion="1.0" productionDate="2006-05-10">
        {
        </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:
<table>
<thead>
<tr>
<th>Element</th>
<th>Description</th>
<th>Mandatory/Optional</th>
</tr>
</thead>
<tbody>
<tr>
<td>ApplicationIdentification</td>
<td>The application identification for which the sequence listing is submitted</td>
<td>Mandatory when a sequence listing is furnished at any time following the assignment of the application number</td>
</tr>
<tr>
<td>IPOfficeCode</td>
<td>ST.3 Code of the office of filing</td>
<td>Mandatory</td>
</tr>
<tr>
<td>ApplicationNumberText</td>
<td>The application identification as provided by the office of filing (e.g., PCT/IB2013/099999)</td>
<td>Mandatory</td>
</tr>
<tr>
<td>FilingDate</td>
<td>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)</td>
<td>Mandatory when a sequence listing is furnished at any time following the assignment of a filing date</td>
</tr>
<tr>
<td>ApplicantFileReference</td>
<td>A single unique identifier assigned by applicant to identify a particular application, typed in the characters as set forth in paragraph 40 (b)</td>
<td>Mandatory when a sequence listing is furnished at any time prior to assignment of the application number; otherwise, Optional</td>
</tr>
<tr>
<td>EarliestPriorityApplicationIdentification</td>
<td>The application identification of the earliest priority claim (also contains IPOfficeCode, ApplicationNumberText and FilingDate, see ApplicationIdentification above)</td>
<td>Mandatory where priority is claimed</td>
</tr>
<tr>
<td>ApplicantName</td>
<td>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.</td>
<td>Mandatory</td>
</tr>
<tr>
<td>ApplicantNameLatin</td>
<td>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)</td>
<td>Mandatory where ApplicantName contains non-Latin characters</td>
</tr>
<tr>
<td>InventorName</td>
<td>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.</td>
<td>Optional</td>
</tr>
<tr>
<td>Element</td>
<td>Description</td>
<td>Mandatory/Optional</td>
</tr>
<tr>
<td>-------------------------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>InventorNameLatin</td>
<td>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)</td>
<td>Optional</td>
</tr>
<tr>
<td>InventionTitle</td>
<td>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 is preferably two to seven words.</td>
<td>Mandatory in the language of filing. Optional for additional languages.</td>
</tr>
<tr>
<td>SequenceTotalQuantity</td>
<td>The total number of all sequences in the sequence listing including intentionally skipped sequences (also known as empty sequences) (see paragraph 10).</td>
<td>Mandatory</td>
</tr>
</tbody>
</table>

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
<?xml version="1.0" encoding="UTF-8"?><!DOCTYPE ST26SequenceListing PUBLIC "+//WIPO//DTD Sequence Listing 1.2//EN" "ST26SequenceListing_V1_2.dtd">
<ST26SequenceListing dtdVersion="V1_2" fileName="Invention_SEQL.xml" softwareName="SEQL-software-name" softwareVersion="1.0" productionDate="2015-05-10">
<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
<?xml version="1.0" encoding="UTF-8"?>
<!DOCTYPE ST26SequenceListing PUBLIC "-//WIPO//DTD Sequence Listing 1.2//EN" "ST26SequenceListing_V1_2.dtd">
<ST26SequenceListing dtdVersion="1_2" fileName="Invention_SEQL.xml" softwareName="SEQL-software-name" softwareVersion="1.0" productionDate="2015-05-10">
  <ApplicationIdentification>
    <IPOfficeCode>US</IPOfficeCode>
    <ApplicationNumberText>14/999,999</ApplicationNumberText>
    <FilingDate>2015-01-05</FilingDate>
  </ApplicationIdentification>
  <ApplicationIdentification>
    <IPOfficeCode>IB</IPOfficeCode>
    <ApplicationNumberText>PCT/IB2014/099999</ApplicationNumberText>
    <FilingDate>2014-07-10</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

```xml
<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:

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

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

<table>
<thead>
<tr>
<th>Element</th>
<th>Description</th>
<th>Mandatory/Not Included</th>
</tr>
</thead>
<tbody>
<tr>
<td>INSDSeq_length</td>
<td>Length of the sequence</td>
<td>Mandatory</td>
</tr>
<tr>
<td>INSDSeq_moltype</td>
<td>Molecule type</td>
<td>Mandatory</td>
</tr>
<tr>
<td>INSDSeq_division</td>
<td>Indication that a sequence is related to a patent application</td>
<td>Mandatory with the value “PAT”</td>
</tr>
<tr>
<td>INSDSeq_feature-table</td>
<td>List of annotations of the sequence</td>
<td>Mandatory</td>
</tr>
<tr>
<td>INSDSeq_sequence</td>
<td>Sequence</td>
<td>Mandatory</td>
</tr>
</tbody>
</table>

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:

```xml
<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 qualifiers “mol_type” and “MOL_TYPE” discussed in paragraphs 55 and 84). For example:

```xml
<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:

```xml
<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>
      </INSDFeature_quals>
    </INSDFeature>
  </INSDSeq_feature-table>
</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.
Each INSDFeature element describes one feature, and consists of dependent elements as follows:

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

**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 the “SOURCE” feature key is mandatory for all amino acid sequences, except for any intentionally skipped sequence. Each sequence must have a single “source” or “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, and may contain one or more location operator(s) (see paragraphs 67 to 70).

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

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

<table>
<thead>
<tr>
<th>Location descriptor type</th>
<th>Syntax</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single residue number</td>
<td>x</td>
<td>Points to a single residue in the sequence.</td>
</tr>
<tr>
<td>Residue numbers delimiting a sequence span</td>
<td>x..y</td>
<td>Points to a continuous range of residues bounded by and including the starting and ending residues.</td>
</tr>
<tr>
<td>Residues before the first or beyond the last specified residue number</td>
<td>&lt;x</td>
<td>Points to a region including a specified residue or span of residues and extending beyond a specified residue. The ‘&lt;’ and ‘&gt;’ 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.</td>
</tr>
<tr>
<td></td>
<td>&gt;x</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;x..y</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;x..&gt;y</td>
<td></td>
</tr>
<tr>
<td>A site between two adjoining residue numbers</td>
<td>x^y</td>
<td>Points to a site between two adjoining residues, e.g., endonucleolytic cleavage site. The position numbers for the adjacent residues 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.</td>
</tr>
</tbody>
</table>

en / 03-26-01
Date: September 2019
67. 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.

(a) Location operator for nucleotides and amino acids:

<table>
<thead>
<tr>
<th>Location syntax</th>
<th>Location description</th>
</tr>
</thead>
<tbody>
<tr>
<td>join(location, location, ... location)</td>
<td>The indicated locations are joined (placed end-to-end) to form one contiguous sequence.</td>
</tr>
<tr>
<td>order(location, location, ... location)</td>
<td>The elements are found in the specified order but nothing is implied about whether joining those elements is reasonable.</td>
</tr>
</tbody>
</table>

(b) Location operator for nucleotides only:

<table>
<thead>
<tr>
<th>Location syntax</th>
<th>Location description</th>
</tr>
</thead>
<tbody>
<tr>
<td>complement(location)</td>
<td>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.</td>
</tr>
</tbody>
</table>

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 for nucleotides only. “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 nucleotides and amino acids:

<table>
<thead>
<tr>
<th>Location Example</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>467</td>
<td>Points to residue 467 in the sequence.</td>
</tr>
<tr>
<td>123^124</td>
<td>Points to a site between residues 123 and 124.</td>
</tr>
<tr>
<td>340..565</td>
<td>Points to a continuous range of residues bounded by and including residues 340 and 565.</td>
</tr>
<tr>
<td>&lt;1</td>
<td>Points to a feature location before the first residue.</td>
</tr>
<tr>
<td>&lt;345..500</td>
<td>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.</td>
</tr>
<tr>
<td>&lt;1..888</td>
<td>Indicates that the feature starts before the first sequence residue and continues to and includes residue 888.</td>
</tr>
<tr>
<td>1..&gt;888</td>
<td>Indicates that the feature starts at the first sequenced residue and continues beyond residue 888.</td>
</tr>
<tr>
<td>join(12..78,134..202)</td>
<td>Indicates that regions 12 to 78 and 134 to 202 should be joined to form one contiguous sequence.</td>
</tr>
</tbody>
</table>
(b) locations for nucleotides only:

<table>
<thead>
<tr>
<th>Location example</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>complement(34..126)</td>
<td>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).</td>
</tr>
<tr>
<td>complement(join(2691..4571, 4918..5163))</td>
<td>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).</td>
</tr>
<tr>
<td>join(complement(4918..5163), complement(2691..4571))</td>
<td>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).</td>
</tr>
</tbody>
</table>

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..&gt;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 and 86);
(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 feature key and Section 8 provides the exclusive listing of qualifiers for each amino acid 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.

**Mandatory feature qualifiers**

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

**Qualifier elements**

76. The element **INSDQualifier** contains one or more INSDQualifier elements. Each INSDQualifier element represents a single qualifier and consists of two dependent elements as follows:

<table>
<thead>
<tr>
<th>Element</th>
<th>Description</th>
<th>Mandatory/Optional</th>
</tr>
</thead>
<tbody>
<tr>
<td>INSDQualifier_name</td>
<td>Name of the qualifier (see Annex I, Sections 6 and 8)</td>
<td>Mandatory</td>
</tr>
<tr>
<td>INSDQualifier_value</td>
<td>Value of the qualifier, if any, in the specified format (see Annex I, Sections 6 and 8)</td>
<td>Mandatory, when specified (see Annex I, Sections 6 and 8)</td>
</tr>
</tbody>
</table>

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 the qualifier “NOTE” for amino acid sequences, but must not be used in the organism qualifier value.

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

Example 1: Source for a nucleotide sequence

```xml
<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

```xml
<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:

```xml
<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:

```xml
<INSDQualifier_name>organism</INSDQualifier_name>
<INSDQualifier_value>unidentified</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:

```xml
<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:

```xml
<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>
```

84. The “mol_type” qualifier for nucleotide sequences (see Annex I, Section 6) and “MOL_TYPE” 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 is a type of value format for certain qualifiers (as indicated in Annex I), presented in the form of a descriptive text phrase that should preferably be in the English language.

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, the free text must not exceed 1000 characters.

Coding sequences

87. 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.

88. 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 5) is assumed.

89. 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.

90. An amino acid sequence encoded by the 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:

```xml
<INSDFeature>
  <INSDFeature_key>CDS</INSDFeature_key>
  <INSDFeature_location>1..50</INSDFeature_location>
  <INSDFeature_quals>
    <INSDQualifier>
      <INSDQualifier_name>transl_table</INSDQualifier_name>
    </INSDQualifier>
  </INSDFeature_quals>
</INSDFeature>
```
Variants

91. 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.

92. Any variant sequence, disclosed as a single sequence with enumerated alternative variant 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 variant residues are represented by the most restrictive ambiguity symbol (see paragraphs 15 and 27).

93. 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).

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

<table>
<thead>
<tr>
<th>Type of sequence</th>
<th>Feature Key</th>
<th>Qualifier</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nucleic acid</td>
<td>variation</td>
<td>replace or note</td>
<td>Naturally occurring mutations and polymorphisms, e.g., alleles, RFLPs.</td>
</tr>
<tr>
<td>Nucleic acid</td>
<td>misc_difference</td>
<td>replace or note</td>
<td>Variability introduced artificially, e.g., by genetic manipulation or by chemical synthesis.</td>
</tr>
<tr>
<td>Amino acid</td>
<td>VAR_SEQ</td>
<td>NOTE</td>
<td>Variant produced by alternative splicing, alternative promoter usage, alternative initiation and ribosomal frameshifting.</td>
</tr>
<tr>
<td>Amino acid</td>
<td>VARIANT</td>
<td>NOTE</td>
<td>Any type of variant for which VAR_SEQ is not applicable.</td>
</tr>
</tbody>
</table>
95. 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 variant residues may be provided as the value in the “note” or “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, but represents a subgroup of “any one of ‘A’, ‘R’, ‘N’, ‘D’, ‘C’, ‘Q’, ‘E’, ‘G’, ‘H’, ‘I’, ‘K’, ‘M’, ‘F’, ‘P’, ‘O’, ‘S’, ‘U’, ‘T’, ‘W’, ‘Y’, or ‘V’”. A deletion must be represented by an empty qualifier value for the “replace” qualifier or by an indication in the “note” or “NOTE” qualifier that the residue may be deleted. An inserted or substituted residue(s) must be provided in the “replace”, “note”, or “NOTE” qualifier. The value format for the “replace”, “note”, and “NOTE” qualifiers is free text and must not exceed 1000 characters, as provided in paragraph 86. See paragraph 98 for sequences encompassed by paragraph 7 that are provided as an insertion or a substitution in a qualifier value.

96. 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” or “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.

97. The following examples illustrate the representation of variants as per paragraphs 93 to 96 above:

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

```xml
<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>
```

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

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

```xml
<INSDFeature>
  <INSDFeature_key>misc_difference</INSDFeature_key>
  <INSDFeature_location>100-101</INSDFeature_location>
  <INSDFeature_quals>
  </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.

```xml
<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.

```xml
<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>
```

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.

```xml
<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>
```

98. 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 1.3

Revision approved by the Committee on WIPO Standards (CWS)
at its seventh session on July 5, 2019

TABLE OF CONTENTS

SECTION 1: LIST OF NUCLEOTIDES ................................................................. 2
SECTION 2: LIST OF MODIFIED NUCLEOTIDES ....................................... 2
SECTION 3: LIST OF AMINO ACIDS ............................................................... 4
SECTION 4: LIST OF MODIFIED AMINO ACIDS ........................................ 5
SECTION 5: FEATURE KEYS FOR NUCLEOTIDE SEQUENCES .................. 6
SECTION 6: QUALIFIERS FOR NUCLEOTIDE SEQUENCES ..................... 25
SECTION 7: FEATURE KEYS FOR AMINO ACID SEQUENCES .................... 50
SECTION 8: QUALIFIERS FOR AMINO ACID SEQUENCES ....................... 57
SECTION 9: GENETIC CODE TABLES .............................................................. 58
SECTION 1: LIST OF NUCLEOTIDES

The nucleotide base codes 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

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Nucleotide</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>adenine</td>
</tr>
<tr>
<td>c</td>
<td>cytosine</td>
</tr>
<tr>
<td>g</td>
<td>guanine</td>
</tr>
<tr>
<td>t</td>
<td>thymine in DNA/uracil in RNA (t/u)</td>
</tr>
<tr>
<td>m</td>
<td>a or c</td>
</tr>
<tr>
<td>r</td>
<td>a or g</td>
</tr>
<tr>
<td>w</td>
<td>a or t/u</td>
</tr>
<tr>
<td>s</td>
<td>c or g</td>
</tr>
<tr>
<td>y</td>
<td>c or t/u</td>
</tr>
<tr>
<td>k</td>
<td>g or t/u</td>
</tr>
<tr>
<td>v</td>
<td>a or c or g; not t/u</td>
</tr>
<tr>
<td>h</td>
<td>a or c or t/u; not g</td>
</tr>
<tr>
<td>d</td>
<td>a or g or t/u; not c</td>
</tr>
<tr>
<td>b</td>
<td>c or g or t/u; not a</td>
</tr>
<tr>
<td>n</td>
<td>a or c or g or t/u; &quot;unknown&quot; or &quot;other&quot;</td>
</tr>
</tbody>
</table>

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 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

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Modified Nucleotide</th>
</tr>
</thead>
<tbody>
<tr>
<td>ac4c</td>
<td>4-acetylcytidine</td>
</tr>
<tr>
<td>chm5u</td>
<td>5-(carboxyhydroxymethyl)uridine</td>
</tr>
<tr>
<td>cm</td>
<td>2'-O-methylcytidine</td>
</tr>
<tr>
<td>cmnm5s2u</td>
<td>5-carboxymethylaminomethyl-2-thioridine</td>
</tr>
<tr>
<td>cmnm5u</td>
<td>5-carboxymethylaminomethyluridine</td>
</tr>
<tr>
<td>dhu</td>
<td>dihydrouridine</td>
</tr>
<tr>
<td>fm</td>
<td>2'-O-methylpseudouridine</td>
</tr>
<tr>
<td>gal q</td>
<td>beta-D-galactosylqueuosine</td>
</tr>
<tr>
<td>gm</td>
<td>2'-O-methylguanosine</td>
</tr>
<tr>
<td>i</td>
<td>inosine</td>
</tr>
<tr>
<td>i6a</td>
<td>N6-isopentenyladenosine</td>
</tr>
<tr>
<td>m1a</td>
<td>1-methyladenosine</td>
</tr>
<tr>
<td>m1f</td>
<td>1-methylpseudouridine</td>
</tr>
<tr>
<td>m1g</td>
<td>1-methylguanosine</td>
</tr>
<tr>
<td>m1i</td>
<td>1-methylinosine</td>
</tr>
<tr>
<td>m22g</td>
<td>2,2-dimethylguanosine</td>
</tr>
<tr>
<td>m2a</td>
<td>2-methyladenosine</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Modified Nucleotide</td>
</tr>
<tr>
<td>--------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>m2g</td>
<td>2-methylguanosine</td>
</tr>
<tr>
<td>m3c</td>
<td>3-methylcytidine</td>
</tr>
<tr>
<td>m4c</td>
<td>N4-methylcytosine</td>
</tr>
<tr>
<td>m5c</td>
<td>5-methylcytidine</td>
</tr>
<tr>
<td>m6a</td>
<td>N6-methyladenosine</td>
</tr>
<tr>
<td>m7g</td>
<td>7-methylguanosine</td>
</tr>
<tr>
<td>mam5u</td>
<td>5-methylaminomethyluridine</td>
</tr>
<tr>
<td>mam5s2u</td>
<td>5-methylaminomethyl-2-thiouridine</td>
</tr>
<tr>
<td>man q</td>
<td>beta-D-mannosylqueuosine</td>
</tr>
<tr>
<td>mcm5s2u</td>
<td>5-methoxycarbonylmethyl-2-thiouridine</td>
</tr>
<tr>
<td>mcm5u</td>
<td>5-methoxycarbonylmethyluridine</td>
</tr>
<tr>
<td>mo5u</td>
<td>5-methoxyuridine</td>
</tr>
<tr>
<td>ms2t6a</td>
<td>2-methylthio-N6-isopentenyladenosine</td>
</tr>
<tr>
<td>ms2t6a</td>
<td>N-((9-beta-D-ribofuranosyl-2-methylthiopurine-6-yl)carbamoyl)threonine</td>
</tr>
<tr>
<td>mt6a</td>
<td>N-((9-beta-D-ribofuranosylpurine-6-yl)N-methyl-carbamoyl)threonine</td>
</tr>
<tr>
<td>mv</td>
<td>uridine-5-oxoacetic acid-methylester</td>
</tr>
<tr>
<td>o5u</td>
<td>uridine-5-oxyacetic acid (v)</td>
</tr>
<tr>
<td>osyw</td>
<td>wybutoxosine</td>
</tr>
<tr>
<td>p</td>
<td>pseudouridine</td>
</tr>
<tr>
<td>q</td>
<td>queuosine</td>
</tr>
<tr>
<td>s2c</td>
<td>2-thiocytidine</td>
</tr>
<tr>
<td>s2t</td>
<td>5-methyl-2-thiouridine</td>
</tr>
<tr>
<td>s2u</td>
<td>2-thiouridine</td>
</tr>
<tr>
<td>s4u</td>
<td>4-thiouridine</td>
</tr>
<tr>
<td>m5u</td>
<td>5-methyluridine</td>
</tr>
<tr>
<td>t6a</td>
<td>N-((9-beta-D-ribofuranosylpurine-6-yl)carbamoyl)threonine</td>
</tr>
<tr>
<td>tm</td>
<td>2’-O-methyl-5-methyluridine</td>
</tr>
<tr>
<td>um</td>
<td>2’-O-methyluridine</td>
</tr>
<tr>
<td>yw</td>
<td>wybutosine</td>
</tr>
<tr>
<td>x</td>
<td>3-(3-amino-3-carboxypropyl)uridine, (acp3)u</td>
</tr>
<tr>
<td>OTHER</td>
<td>(requires note qualifier)</td>
</tr>
</tbody>
</table>
SECTION 3: LIST OF AMINO ACIDS

The amino acid codes 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 "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

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

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Modified Amino acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aad</td>
<td>2-Aminoadipic acid</td>
</tr>
<tr>
<td>bAad</td>
<td>3-Aminoadipic acid</td>
</tr>
<tr>
<td>bAla</td>
<td>beta-Alanine, beta-Aminoproprionic acid</td>
</tr>
<tr>
<td>Abu</td>
<td>2-Aminobutyric acid</td>
</tr>
<tr>
<td>4Abu</td>
<td>4-Aminobutyric acid, piperidinic acid</td>
</tr>
<tr>
<td>Acp</td>
<td>6-Aminocaproic acid</td>
</tr>
<tr>
<td>Ahe</td>
<td>2-Aminoheptanoic acid</td>
</tr>
<tr>
<td>Alb</td>
<td>2-Aminoisobutyric acid</td>
</tr>
<tr>
<td>bAlb</td>
<td>3-Aminoisobutyric acid</td>
</tr>
<tr>
<td>Apm</td>
<td>2-Aminopimelic acid</td>
</tr>
<tr>
<td>Dbu</td>
<td>2,4-Diaminobutyric acid</td>
</tr>
<tr>
<td>Des</td>
<td>Desmosine</td>
</tr>
<tr>
<td>Dpm</td>
<td>2,2’-Diaminopimelic acid</td>
</tr>
<tr>
<td>Dpr</td>
<td>2,3-Diaminoproprionic acid</td>
</tr>
<tr>
<td>EtGly</td>
<td>N-Ethylglycine</td>
</tr>
<tr>
<td>EtAsn</td>
<td>N-Ethylasparagine</td>
</tr>
<tr>
<td>Hyl</td>
<td>Hydroxylysine</td>
</tr>
<tr>
<td>aHyl</td>
<td>allo-Hydroxylysine</td>
</tr>
<tr>
<td>3Hyp</td>
<td>3-Hydroxyproline</td>
</tr>
<tr>
<td>4Hyp</td>
<td>4-Hydroxyproline</td>
</tr>
<tr>
<td>Ide</td>
<td>Isodesmosine</td>
</tr>
<tr>
<td>aIle</td>
<td>allo-Isoleucine</td>
</tr>
<tr>
<td>MeGly</td>
<td>N-Methylglycine, sarcosine</td>
</tr>
<tr>
<td>MeIle</td>
<td>N-Methylisoleucine</td>
</tr>
<tr>
<td>MeLys</td>
<td>6-N-Methyllysine</td>
</tr>
<tr>
<td>MeVal</td>
<td>N-Methylvaline</td>
</tr>
<tr>
<td>Nva</td>
<td>Norvaline</td>
</tr>
<tr>
<td>Nle</td>
<td>Norleucine</td>
</tr>
<tr>
<td>Orn</td>
<td>Ornithine</td>
</tr>
</tbody>
</table>
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 |
§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 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, pseudogene 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

§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
### §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. 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

### §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
### §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.

### §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
- pseudo
- pseudogene
- standard_name

**Molecule scope:** DNA

**Comment:** E.g., in the somatic processing of immunoglobulin genes.

### §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: joining_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
close
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
<table>
<thead>
<tr>
<th>Feature Key</th>
<th>Definition</th>
<th>Mandatory qualifiers</th>
<th>Optional qualifiers</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>modified_base</td>
<td>the indicated nucleotide is a modified nucleotide and should be substituted for by the indicated molecule (given in the mod_base qualifier value)</td>
<td>mod_base</td>
<td>allele, frequency, gene, gene_synonym, map, note</td>
<td>value for the mandatory mod_base qualifier is limited to the restricted vocabulary for modified base abbreviations in Section 2 of this Annex.</td>
</tr>
<tr>
<td>mRNA</td>
<td>messenger RNA; includes 5' untranslated region (5' UTR), coding sequences (CDS, exon) and 3' untranslated region (3' UTR)</td>
<td></td>
<td>allele, function, gene, gene_synonym, map, note, operon, product, pseudo, pseudogene, standard_name, trans_splicing</td>
<td></td>
</tr>
<tr>
<td>ncRNA</td>
<td>a non-protein-coding gene, other than ribosomal RNA and transfer RNA, the functional molecule of which is the RNA transcript</td>
<td>ncRNA_class</td>
<td>allele, function, gene, gene_synonym, map, note, operon, product, pseudo, pseudogene, standard_name, trans_splicing</td>
<td>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</td>
</tr>
</tbody>
</table>
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
<table>
<thead>
<tr>
<th>Feature Key</th>
<th>Definition</th>
<th>Optional Qualifiers</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>primer_bind</td>
<td>non-covalent primer binding site for initiation of replication, transcription, or reverse transcription; includes site(s) for synthetic e.g., PCR primer elements</td>
<td>allele, gene, gene_synonym, map, note, standard_name</td>
<td>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</td>
</tr>
<tr>
<td>propeptide</td>
<td>propeptide coding sequence; coding sequence for the domain of a preprotein that is cleaved to form the mature protein product.</td>
<td>allele, function, gene, gene_synonym, map, note, product, pseudo, pseudogene, standard_name</td>
<td></td>
</tr>
<tr>
<td>protein_bind</td>
<td>non-covalent protein binding site on nucleic acid</td>
<td>bound_moiety, allele, function, gene, gene_synonym, map, note, operon, standard_name</td>
<td>note that the regulatory feature key and regulatory_class qualifier with the value “ribosome_binding_site” must be used to describe ribosome binding sites</td>
</tr>
</tbody>
</table>
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
### 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.

### 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.

### 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.
### 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
- germine
- hapl_group
- hapl_type
- 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: stemloop

**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, anticodon, function, gene, gene_synonym, map, note, operon, product, pseudo, pseudogene, standard_name, trans_splicing.
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 un-called-bases ('n').

Optional qualifiers allele
compact
gene
gene_synonym
map
note
replace

Comment use the replace qualifier to annotate a deletion, insertion, or substitution.

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

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
§ 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

§ 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 "&apos;" in the value of an element. Thus "3' UTR" must be represented as "3apos; UTR" in the XML file, i.e., <NSDFeature_key>3apos; UTR</NSDFeature_key>.
<table>
<thead>
<tr>
<th>Feature Key</th>
<th>5' UTR</th>
</tr>
</thead>
</table>

**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 “&apos;” in the value of an element. Thus “5’UTR” must be represented as “$5apos;UTR” in the XML file, i.e., <NSDFeature_key>5apos;UTR</NSDFeature_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 a Value format of “none” is indicated in the description of a qualifier (e.g., germline), the INSDQualifier_value element must not be used.

PLEASE NOTE: Any qualifier value provided for a qualifier with a “free text” value format may require translation for National/Regional procedures.

6.1. Qualifier allele

Definition name of the allele for the given gene

Value format free text

(Note: this value may require translation for National/Regional procedures)

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

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>

6.3. Qualifier bound_moiety

Definition name of the molecule/complex that may bind to the given feature

Value format free text

(Note: this value may require translation for 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

**Value format**
free text
(NOTE: this value may require translation for National/Regional procedures)

**Example**
\(<\text{INSDQualifier_value}>\text{MCF7}\text{\textunderscore}\text{INSDQualifier_value}>\)

6.5. **Qualifier** cell_type

**Definition**
cell type from which the sequence was obtained

**Value format**
free text
(NOTE: this value may require translation for National/Regional procedures)

**Example**
\(<\text{INSDQualifier_value}>\text{leukocyte}\text{\textunderscore}\text{INSDQualifier_value}>\)

6.6. **Qualifier** chromosome

**Definition**
chromosome (e.g., Chromosome number) from which the sequence was obtained

**Value format**
free text
(NOTE: this value may require translation for National/Regional procedures)

**Example**
\(<\text{INSDQualifier_value}>\text{1}\text{\textunderscore}\text{INSDQualifier_value}>\)
\(<\text{INSDQualifier_value}>\text{X}\text{\textunderscore}\text{INSDQualifier_value}>\)

6.7. **Qualifier** clone

**Definition**
clone from which the sequence was obtained

**Value format**
free text
(NOTE: this value may require translation for National/Regional procedures)

**Example**
\(<\text{INSDQualifier_value}>\text{lambda\textunderscore}h\text{\_IL7}\text{.3}\text{\textunderscore}\text{INSDQualifier_value}>\)

**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.

6.8. **Qualifier** clone_lib

**Definition**
clone library from which the sequence was obtained

**Value format**
free text
(NOTE: this value may require translation for National/Regional procedures)

**Example**
\(<\text{INSDQualifier_value}>\text{lambda\textunderscore}h\text{\_IL7}\text{\_inSDQualifier_value}>\)
<table>
<thead>
<tr>
<th>Section</th>
<th>Qualifier</th>
<th>Definition</th>
<th>Value format</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.9</td>
<td>codon_start</td>
<td>indicates the offset at which the first complete codon of a coding feature can be found, relative to the first base of that feature.</td>
<td>1 or 2 or 3</td>
<td><code>&lt;INSDQualifier_value&gt;2&lt;/INSDQualifier_value&gt;</code></td>
</tr>
<tr>
<td>6.10</td>
<td>collected_by</td>
<td>name of persons or institute who collected the specimen</td>
<td>free text</td>
<td><code>&lt;INSDQualifier_value&gt;Dan Janzen&lt;/INSDQualifier_value&gt;</code></td>
</tr>
<tr>
<td>6.11</td>
<td>collection_date</td>
<td>date that the specimen was collected.</td>
<td>YYYY-MM-DD, YYYY-MM or YYYY</td>
<td><code>&lt;INSDQualifier_value&gt;1952-10-21&lt;/INSDQualifier_value&gt;</code>&lt;br&gt;<code>&lt;INSDQualifier_value&gt;1952-10&lt;/INSDQualifier_value&gt;</code>&lt;br&gt;<code>&lt;INSDQualifier_value&gt;1952&lt;/INSDQualifier_value&gt;</code></td>
</tr>
<tr>
<td>6.12</td>
<td>compare</td>
<td>Reference details of an existing public INSD entry to which a comparison is made</td>
<td>[accession-number.sequence-version]</td>
<td><code>&lt;INSDQualifier_value&gt;AJ634337.1&lt;/INSDQualifier_value&gt;</code></td>
</tr>
</tbody>
</table>

Comment:
- 'YYYY' is a four-digit value representing the year. 'MM' is a two-digit value representing the month. 'DD' is a two-digit value representing the day of the month.
- 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.
6.13. **Qualifier**: cultivar

**Definition**: cultivar (cultivated variety) of plant from which sequence was obtained.

**Value format**: free text

*(NOTE: this value may require translation for 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.

6.14. **Qualifier**: dev_stage

**Definition**: if the sequence was obtained from an organism in a specific developmental stage, it is specified with this qualifier.

**Value format**: free text

*(NOTE: this value may require translation for National/Regional procedures)*

**Example**: `<INSDQualifier_value>fourth instar larva</INSDQualifier_value>`

6.15. **Qualifier**: direction

**Definition**: direction of DNA replication

**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.
6.16. Qualifier: EC_number
Definition: Enzyme Commission number for enzyme product of sequence
Value format: free text
(Note: this value may require translation for National/Regional procedures)
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.

6.17. Qualifier: ecotype
Definition: A population within a given species displaying genetically based, phenotypic traits that reflect adaptation to a local habitat
Value format: free text
(Note: this value may require translation for 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.

6.18. 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.
6.19. **Qualifier exception**

**Definition**
indicates that the coding region cannot be translated using standard biological rules

**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.

6.20. **Qualifier frequency**

**Definition**
frequency of the occurrence of a feature

**Value format**
free text representing the proportion of a population carrying the feature expressed as a fraction
(NOTE: this value may require translation for National/Regional procedures)

**Example**
- `<INSDQualifier_value>23/108</INSDQualifier_value>`
- `<INSDQualifier_value>1 in 12</INSDQualifier_value>`
- `<INSDQualifier_value>0.85</INSDQualifier_value>`

6.21. **Qualifier function**

**Definition**
function attributed to a sequence

**Value format**
free text
(NOTE: this value may require translation for 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.

6.22. **Qualifier gene**

**Definition**
symbol of the gene corresponding to a sequence region

**Value format**
free text
(NOTE: this value may require translation for National/Regional procedures)

**Example**
- `<INSDQualifier_value>live</INSDQualifier_value>`

**Comment**
Use gene qualifier to provide the gene symbol; use standard_name qualifier to provide the full gene name.
6.23. **Qualifier**: gene_synonym
   
   **Definition**: synonymous, replaced, obsolete or former gene symbol
   
   **Value format**: free text
   
   *(NOTE: this value may require translation for National/Regional procedures)*
   
   **Example**: &lt;INSQualifier_value&gt;Hox-3.3&lt;/INSQualifier_value&gt; 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

6.24. **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=86593)

6.25. **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.
   
   **Value format**: free text
   
   *(NOTE: this value may require translation for National/Regional procedures)*
   
   **Example**: &lt;INSQualifier_value&gt;H*&lt;/INSQualifier_value&gt;

6.26. **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.
   
   **Value format**: free text
   
   *(NOTE: this value may require translation for National/Regional procedures)*
   
   **Example**: &lt;INSQualifier_value&gt;Dw3 B5 Cw1 A1&lt;/INSQualifier_value&gt;
6.27. **Qualifier**  
**host**  
**Definition**  natural (as opposed to laboratory) host to the organism from which sequenced molecule was obtained  
**Value format**  free text  
(NOTE: this value may require translation for 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>  

6.28. **Qualifier**  
**identified_by**  
**Definition**  name of the expert who identified the specimen taxonomically  
**Value format**  free text  
(NOTE: this value may require translation for National/Regional procedures)  
**Example**  
<INSDQualifier_value>John Burns</INSDQualifier_value>  

6.29. **Qualifier**  
**isolate**  
**Definition**  individual isolate from which the sequence was obtained  
**Value format**  free text  
(NOTE: this value may require translation for National/Regional procedures)  
**Example**  
<INSDQualifier_value>Patient #152</INSDQualifier_value>  
<INSDQualifier_value>DGGE band PSBAC-13</INSDQualifier_value>  

6.30. **Qualifier**  
**isolation_source**  
**Definition**  describes the physical, environmental and/or local geographical source of the biological sample from which the sequence was derived  
**Value format**  free text  
(NOTE: this value may require translation for 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
### 6.31. Qualifier: lab_host

**Definition:** scientific name of the laboratory host used to propagate the source organism from which the sequenced molecule was obtained.

**Value format:** free text

*(NOTE: this value may require translation for 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.

### 6.32. Qualifier: lat_lon

**Definition:** geographical coordinates of the location where the specimen was collected.

**Value format:** free text - degrees latitude and longitude in format "d[d.dddd] N|S d[dd.dddd] W|E" (NOTE: this value may require translation for National/Regional procedures)

**Example:**
- `<INSDQualifier_value>47.94 N 28.12 W</INSDQualifier_value>`
- `<INSDQualifier_value>45.0123 S 4.1234 E</INSDQualifier_value>`

### 6.33. 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

### 6.34. Qualifier: map

**Definition:** genomic map position of feature.

**Value format:** free text (NOTE: this value may require translation for National/Regional procedures)

**Example:** `<INSDQualifier_value>8q12-q13</INSDQualifier_value>`
6.35. **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.

**Value format**: free text

*(NOTE: this value may require translation for 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.

6.36. **Qualifier**: mobile_element_type

**Definition**: type and name or identifier of the mobile element which is described by the parent feature.

**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 only. Mobile elements 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>`.

6.37. **Qualifier**: mod_base

**Definition**: abbreviation for a modified nucleotide base.

**Value format**: modified base abbreviation chosen from this Annex, Section 2.

**Example**: `<INSDQualifier_value>m5c</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 as its value.
6.38. **Qualifier**: mol_type

**Definition**: molecule type of sequence

**Value format**: One chosen from the following:
- genomic DNA
- genomic RNA
- tRNA
- rRNA
- other RNA
- other DNA
- transcribed RNA
- viral cRNA
- unassigned DNA
- unassigned RNA

**Example**: `<INSDQualifier_value>genomic DNA</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.
6.39. Qualifier

cRNA_class

Definition

A structured description of the classification of the non-coding RNA described by the ncRNA parent key.

Value format

TYPE

where TYPE is one of the following controlled vocabulary terms or phrases:

- antisense_RNA
- autocatalytically_spliced_intron
- ribozyme
- hammerhead_ribozyme
- lncRNA
- RNase_P_RNA
- RNase_MRP_RNA
- telomerase_RNA
- guide_RNA
- sgRNA
- rasiRNA
- scRNA
- scaRNA
- 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.

6.40. Qualifier

note

Definition

Any comment or additional information.

Value format

free text

(NOTE: this value may require translation for National/Regional procedures)

Example

<INSDQualifier_value>A comment about the feature</INSDQualifier_value>
6.41. Qualifier 

**Definition**
a number to indicate the order of genetic elements (e.g., exons or introns) in the 5' to 3' direction

**Value format**
free text (with no whitespace characters)

*(NOTE: this value may require translation for National/Regional procedures)*

**Example**

\(<\text{INSDQualifier\_value}>4</\text{INSDQualifier\_value}>\)

\(<\text{INSDQualifier\_value}>6B</\text{INSDQualifier\_value}>\)

**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"

6.42. Qualifier 

**Definition**
name of the group of contiguous genes transcribed into a single transcript to which that feature belongs

**Value format**
free text

*(NOTE: this value may require translation for National/Regional procedures)*

**Example**

\(<\text{INSDQualifier\_value}>lac</\text{INSDQualifier\_value}>\)

6.43. Qualifier 

**Definition**
type of membrane-bound intracellular structure from which the sequence was obtained

**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**

\(<\text{NSDQualifier\_value}>\text{chromatophore}/</\text{NSDQualifier\_value}>\)

\(<\text{NSDQualifier\_value}>\text{hydrogenosome}/</\text{NSDQualifier\_value}>\)

\(<\text{NSDQualifier\_value}>\text{mitochondrion}/</\text{NSDQualifier\_value}>\)

\(<\text{NSDQualifier\_value}>\text{nucleomorph}/</\text{NSDQualifier\_value}>\)

\(<\text{NSDQualifier\_value}>\text{plastid}/</\text{NSDQualifier\_value}>\)

\(<\text{NSDQualifier\_value}>\text{plastid:kinetoplast}/</\text{NSDQualifier\_value}>\)

\(<\text{NSDQualifier\_value}>\text{plastid:chloroplast}/</\text{NSDQualifier\_value}>\)

\(<\text{NSDQualifier\_value}>\text{plastid:apicoplast}/</\text{NSDQualifier\_value}>\)

\(<\text{NSDQualifier\_value}>\text{plastid:chromoplast}/</\text{NSDQualifier\_value}>\)

\(<\text{NSDQualifier\_value}>\text{plastid:cyanelle}/</\text{NSDQualifier\_value}>\)

\(<\text{NSDQualifier\_value}>\text{plastid:leucoplast}/</\text{NSDQualifier\_value}>\)

\(<\text{NSDQualifier\_value}>\text{plastid:proplastid}/</\text{NSDQualifier\_value}>\)
6.44. **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

**Value format**
free text

*(NOTE: this value may require translation for National/Regional procedures)*

**Example**

```xml
<INSDQualifier_value>Homo sapiens</INSDQualifier_value>
```

6.45. **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

**Value format**

```
```

**Example**

```xml
<INSDQualifier_value>
  fwd_name: CO1P1, fwd_seq: ttgattttttgtcayccwgaagt, rev_name: CO1R4, rev_seq: ccwytardctararagtgttg
</INSDQualifier_value>

<INSDQualifier_value>
  fwd_name: hoge1, fwd_seq: cgkgtgtatcttact, rev_name: hoge2, rev_seq: cg&lt;i&gt;gtgtatcttact
</INSDQualifier_value>

<INSDQualifier_value>
  fwd_name: CO1P1, fwd_seq: ttgattttttgtcayccwgaagt, fwd_name: CO1P2, fwd_seq: gatacacaggtcayccwgaagt, rev_name: CO1R4, rev_seq: ccwytardctararagtgttg
</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’>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 &lt; and &gt; since they are reserved characters in XML.

6.46. **Qualifier phenotype**

**Definition**
phenotype conferred by the feature, where phenotype is defined as a physical, biochemical or behavioural characteristic or set of characteristics

**Value format**
free text

*(NOTE: this value may require translation for National/Regional procedures)*

**Example**

```xml
<INSDQualifier_value>erythromycin resistance</INSDQualifier_value>
```

6.47. **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

**Value format**
free text

*(NOTE: this value may require translation for National/Regional procedures)*

**Example**

```xml
<INSDQualifier_value>pC589</INSDQualifier_value>
```
6.48. Qualifier: pop_variant

Definition: name of subpopulation or phenotype of the sample from which the sequence was derived.

Value format: free text

(Note: this value may require translation for National/Regional procedures)

Example: <INSDQualifier_value>pop1</INSDQualifier_value>
<INSDQualifier_value>Bear Paw</INSDQualifier_value>

6.49. 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.

Value format: free text

(Note: this value may require translation for 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)

6.50. 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.

Value format: an integer greater than zero

Example: <INSDQualifier_value>89</INSDQualifier_value>

6.51. 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

6.52. 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.
6.53. **Qualifier**: pseudogene

**Definition**: Indicates that this feature is a pseudogene of the element named by the feature key.

**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 an mRNA into cDNA, followed by reinsertion 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, frame shifts, and a higher proportion of non-synonymous versus synonymous substitutions.
- unitary - The pseudogene has no parent. It is the original gene, which is functional in 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.

6.54. **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) loci in the jawless fish (lampreys and hagfish); germline and rearranged qualifiers should not be used outside of the Craniata (taxid=9593).
6.55. **Qualifier** recombination\_class

**Definition**
a structured description of the classification of recombination hotspot region within a sequence

**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

6.56. **Qualifier** regulatory\_class

**Definition**
a structured description of the classification of transcriptional, translational, replicational and chromatin structure related regulatory elements in a sequence

**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
replication\_regulatory\_region
response\_element
ribosome\_binding\_site
riboswitch
silencer
TATA\_box
terminator
transcriptional\_cis\_regulatory\_region
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
6.57. **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.

**Value format** free text

*(NOTE: this value may require translation for National/Regional procedures)*

**Example**

```
<INSDQualifier_value>a</INSDQualifier_value>
<INSDQualifier_value></INSDQualifier_value> - for a deletion
```

6.58. **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.

6.59. **Qualifier** rpt_family

**Definition** type of repeated sequence; "Alu" or "Kpn", for example

**Value format** free text

*(NOTE: this value may require translation for National/Regional procedures)*

**Example**

```
<INSDQualifier_value>Alu</INSDQualifier_value>
```
6.60. **Qualifier** rpt_type

**Definition**
structure and distribution of repeated sequence

**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.

6.61. **Qualifier** rpt_unit_range

**Definition**
location of a repeating unit expressed as a range

**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.
6.62. Qualifier rpt_unit_seq
Definition identity of a repeat sequence
Value format free text
(NOTE: this value may require translation for National/Regional procedures)
Example<br>
\(<\text{INSDQualifier_value}>aagggc</\text{INSDQualifier_value}>\)<br>
\(<\text{INSDQualifier_value}>ag(5)tg(8)</\text{INSDQualifier_value}>\)<br>
\(<\text{INSDQualifier_value}>\text{AAAGA}6\text{AAAA}1\text{AAAGA}12</\text{INSDQualifier_value}>\)<br>
Comment used to indicate the literal sequence that constitutes a repeating unit within the region specified by the feature keys oriT and repeat_region

6.63. Qualifier satellite
Definition identifier for a satellite DNA marker, composed of many tandem repeats (identical or related) of a short basic repeated unit
Value format <satellite_type>:<class>[<identifier>] - where <satellite_type> is one of the following:
satellite; microsatellite; minisatellite
Example<br>
\(<\text{INSDQualifier_value}>\text{satellite}:S1a</\text{INSDQualifier_value}>\)<br>
\(<\text{INSDQualifier_value}>\text{satellite}:\text{alpha}</\text{INSDQualifier_value}>\)<br>
\(<\text{INSDQualifier_value}>\text{satellite}:\text{gamma III}</\text{INSDQualifier_value}>\)<br>
\(<\text{INSDQualifier_value}>\text{microsatellite}:DC130</\text{INSDQualifier_value}>\)<br>
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.

6.64. Qualifier segment
Definition name of viral or phage segment sequenced
Value format free text
(NOTE: this value may require translation for National/Regional procedures)
Example <INSDQualifier_value>6</INSDQualifier_value>

6.65. Qualifier serotype
Definition serological variety of a species characterized by its antigenic properties
Value format free text
(NOTE: this value may require translation for 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"
<table>
<thead>
<tr>
<th>Qualifier</th>
<th>Definition</th>
<th>Value format</th>
<th>Example</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>6.66.</strong> Qualifier</td>
<td>serovar</td>
<td>serological variety of a species (usually a prokaryote) characterized by its antigenic properties</td>
<td>free text&lt;br&gt;(NOTE: this value may require translation for National/Regional procedures)</td>
<td>&lt;INSDQualifier_value&gt;O157:H7&lt;/INSDQualifier_value&gt;</td>
</tr>
<tr>
<td><strong>6.67.</strong> Qualifier</td>
<td>sex</td>
<td>sex of the organism from which the sequence was obtained; sex is used for eukaryotic organisms that undergo meiosis and have sexually dimorphic gametes</td>
<td>free text&lt;br&gt;(NOTE: this value may require translation for National/Regional procedures)</td>
<td>&lt;INSDQualifier_value&gt;female&lt;/INSDQualifier_value&gt;&lt;br&gt;&lt;INSDQualifier_value&gt;male&lt;/INSDQualifier_value&gt;&lt;br&gt;&lt;INSDQualifier_value&gt;hermaphrodite&lt;/INSDQualifier_value&gt;&lt;br&gt;&lt;INSDQualifier_value&gt;unisexual&lt;/INSDQualifier_value&gt;&lt;br&gt;&lt;INSDQualifier_value&gt;bisexual&lt;/INSDQualifier_value&gt;&lt;br&gt;&lt;INSDQualifier_value&gt;sexual&lt;/INSDQualifier_value&gt;&lt;br&gt;&lt;INSDQualifier_value&gt;monoeious&lt;/INSDQualifier_value&gt;&lt;br&gt;&lt;INSDQualifier_value&gt;monoecious&lt;/INSDQualifier_value&gt;&lt;br&gt;&lt;INSDQualifier_value&gt;dioecious&lt;/INSDQualifier_value&gt;</td>
</tr>
<tr>
<td><strong>6.68.</strong> Qualifier</td>
<td>standard_name</td>
<td>accepted standard name for this feature</td>
<td>free text&lt;br&gt;(NOTE: this value may require translation for National/Regional procedures)</td>
<td>&lt;INSDQualifier_value&gt;dotted&lt;/INSDQualifier_value&gt;</td>
</tr>
<tr>
<td>Section</td>
<td>Qualifier</td>
<td>Definition</td>
<td>Value format</td>
<td>Example</td>
</tr>
<tr>
<td>---------</td>
<td>-----------</td>
<td>------------</td>
<td>--------------</td>
<td>---------</td>
</tr>
<tr>
<td>6.69.</td>
<td>qualifier</td>
<td>strain</td>
<td>free text</td>
<td><code>&lt;INSDQualifier_value&gt;BALB/c&lt;/INSDQualifier_value&gt;</code></td>
</tr>
<tr>
<td></td>
<td></td>
<td>strain from which sequence was obtained</td>
<td>(NOTE: this value may require translation for National/Regional procedures)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>sub_clone</td>
<td>free text</td>
<td><code>&lt;INSDQualifier_value&gt;lambda-hIL7.20g&lt;/INSDQualifier_value&gt;</code></td>
</tr>
<tr>
<td></td>
<td></td>
<td>sub_species</td>
<td>free text</td>
<td><code>&lt;INSDQualifier_value&gt;lactis&lt;/INSDQualifier_value&gt;</code></td>
</tr>
<tr>
<td></td>
<td></td>
<td>name of sub-species of organism from which sequence was obtained</td>
<td>(NOTE: this value may require translation for National/Regional procedures)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>sub_strain</td>
<td>free text</td>
<td><code>&lt;INSDQualifier_value&gt;abis&lt;/INSDQualifier_value&gt;</code></td>
</tr>
<tr>
<td></td>
<td></td>
<td>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</td>
<td>(NOTE: this value may require translation for National/Regional procedures)</td>
<td></td>
</tr>
</tbody>
</table>
6.73. Qualifier: tag_peptide
   Definition: base location encoding the polypeptide for proteolysis tag of tmRNA and its termination codon
   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: <INSQ_qualified_value>90..122</INSQ_qualified_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

6.74. Qualifier: tissue_lib
   Definition: tissue library from which sequence was obtained
   Value format: free text
   Example: <INSQ_qualified_value>tissue library 772</INSQ_qualified_value>

6.75. Qualifier: tissue_type
   Definition: tissue type from which the sequence was obtained
   Value format: free text
   Example: <INSQ_qualified_value>liver</INSQ_qualified_value>

6.76. Qualifier: transl_except
   Definition: translational exception: single codon the translation of which does not conform to genetic code defined by organism or transl_table.
   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: <INSQ_qualified_value>(pos:213..215, aa:Trp)</INSQ_qualified_value> 
   Example: <INSQ_qualified_value>(pos:462..464, aa:OTHER)</INSQ_qualified_value> 
   Example: <INSQ_qualified_value>(pos:1017, aa:TERM)</INSQ_qualified_value> 
   Example: <INSQ_qualified_value>(pos:2000..2001, aa:TERM)</INSQ_qualified_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'.
6.77. **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

**Value format**
<integer> where <integer> is the number assigned to the genetic code table

**Example**
<NSDQualifier_value>3</NSDQualifier_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.

6.78. **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

6.79. **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

**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>MASTFPWWRGCAGTPLSKGLI MCTW</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.
6.80. **Qualifier**

<table>
<thead>
<tr>
<th>Definition</th>
<th>Variety (= varietas, a formal Linnaean rank) of organism from which sequence was derived.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value format</td>
<td>Free text (NOTE: this value may require translation for National/Regional procedures)</td>
</tr>
<tr>
<td>Example</td>
<td><code>&lt;INSDQualifier_value&gt;insularis&lt;/INSDQualifier_value&gt;</code></td>
</tr>
<tr>
<td>Comment</td>
<td>Use the cultivar qualifier for cultivated plant varieties, i.e., products of artificial selection; varieties other than plant and fungal varietas should be annotated via a note qualifier, e.g., with the value <code>&lt;INSDQualifier_value&gt;breed: Cukorova&lt;/INSDQualifier_value&gt;</code></td>
</tr>
</tbody>
</table>
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.

<table>
<thead>
<tr>
<th>Feature Key</th>
<th>ACT_SITE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definition</td>
<td>Amino acid(s) involved in the activity of an enzyme</td>
</tr>
<tr>
<td>Optional qualifiers</td>
<td>NOTE</td>
</tr>
<tr>
<td>Comment</td>
<td>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.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Feature Key</th>
<th>BINDING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definition</td>
<td>Binding site for any chemical group (co-enzyme, prosthetic group, etc.). The chemical nature of the group is indicated in the NOTE qualifier</td>
</tr>
<tr>
<td>Mandatory qualifiers</td>
<td>NOTE</td>
</tr>
<tr>
<td>Comment</td>
<td>Examples of values for the &quot;NOTE&quot; qualifier: “Heme (covalent)” and “Chloride.” Where appropriate, the features keys CA_BIND, DNA_BIND, METAL, and NP_BIND should be used rather than BINDING.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Feature Key</th>
<th>CA_BIND</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definition</td>
<td>Extent of a calcium binding region</td>
</tr>
<tr>
<td>Optional qualifiers</td>
<td>NOTE</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Feature Key</th>
<th>CARBOHYD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definition</td>
<td>Glycosylation site</td>
</tr>
<tr>
<td>Mandatory qualifiers</td>
<td>NOTE</td>
</tr>
<tr>
<td>Comment</td>
<td>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 &quot;NOTE&quot; 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 &quot;NOTE&quot; qualifier: N-linked (GlcNAc...); O-linked (GlcNAc); O-linked (Glc...); C-linked (Man) partial; O-linked (Ara...).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Feature Key</th>
<th>CHAIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definition</td>
<td>Extent of a polypeptide chain in the mature protein</td>
</tr>
<tr>
<td>Optional qualifiers</td>
<td>NOTE</td>
</tr>
</tbody>
</table>
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, GSDGE -> RI RLR; 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 descriptors in the feature location element are the residue numbers of the cross-linked amino acids in conjunction with the “join” location operator, e.g., “join(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-methyl thionine (Cys-Thr);” and “Glycyl lysine isopeptide (Lys-Gly) (interchain with G Cte r i n 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 disulfide bond, the location descriptors in the feature location element are the residue numbers of the linked cysteines in conjunction with the “join” location operator, e.g., “join(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 DNABIND
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 INITMET
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 INTRANEM
Definition Extent of a region located in a membrane without crossing it
Optional qualifiers NOTE
<table>
<thead>
<tr>
<th>Feature Key</th>
<th>Definition</th>
<th>Mandatory qualifiers</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>LIPID</td>
<td>Covalent binding of a lipid moiety</td>
<td>NOTE</td>
<td>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 &quot;NOTE&quot; qualifier: &quot;N-myristoyl glycine&quot;; &quot;GPI-anchor amidated serine&quot; and &quot;S-diacylglycerol cysteine.&quot;</td>
</tr>
<tr>
<td>METAL</td>
<td>Binding site for a metal ion.</td>
<td>NOTE</td>
<td>The NOTE qualifier indicates the nature of the metal. Examples of values for the &quot;NOTE&quot; qualifier: &quot;Iron (heme axial ligand)&quot; and &quot;Copper&quot;.</td>
</tr>
<tr>
<td>MOD_RES</td>
<td>Posttranslational modification of a residue</td>
<td>NOTE</td>
<td>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 full name. Examples of values for the &quot;NOTE&quot; qualifier: &quot;N-acetylalanine&quot;; &quot;3-Hyp&quot;; and &quot;MeLys&quot; or &quot;N-6-methyllysine&quot;.</td>
</tr>
<tr>
<td>MOTIF</td>
<td>Short (up to 20 amino acids) sequence motif of biological interest</td>
<td>NOTE</td>
<td></td>
</tr>
<tr>
<td>MUTAGEN</td>
<td>Site which has been experimentally altered by mutagenesis</td>
<td>NOTE</td>
<td></td>
</tr>
<tr>
<td>NON_STD</td>
<td>Non-standard amino acid</td>
<td>NOTE</td>
<td>This key describes the occurrence of non-standard amino acids selenocysteine (U) and pyrrolysine (O) in the amino acid sequence.</td>
</tr>
</tbody>
</table>
### 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 qualifier** 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 qualifier** 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 qualifier** NOTE
<table>
<thead>
<tr>
<th>Feature Key</th>
<th>Definition</th>
<th>Optional qualifiers</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>TURN</td>
<td>Secondary structure Turns, for example, H-bonded turn (3-turn, 4-turn or 5-turn)</td>
<td>NOTE</td>
<td>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.</td>
</tr>
<tr>
<td>UNSURE</td>
<td>Uncertainties in the sequence</td>
<td>NOTE</td>
<td>Used to describe region(s) of an amino acid sequence for which the authors are unsure about the sequence presentation.</td>
</tr>
<tr>
<td>VARIANT</td>
<td>Authors report that sequence variants exist</td>
<td>NOTE</td>
<td></td>
</tr>
<tr>
<td>VAR_SEQ</td>
<td>Description of sequence variants produced by alternative splicing, alternative promoter usage, alternative initiation and ribosomal frameshifting</td>
<td>NOTE</td>
<td></td>
</tr>
<tr>
<td>ZN_FING</td>
<td>Extent of a zinc finger region</td>
<td>NOTE</td>
<td>The type of zinc finger is indicated in the NOTE qualifier. For example: “GATA-type” and “NR C4-type”</td>
</tr>
</tbody>
</table>
SECTION 8: QUALIFIERS FOR AMINO ACID SEQUENCES
This section contains the list of allowed qualifiers to be used for amino acid sequences.

PLEASE NOTE: Any qualifier value provided for a qualifier with a "free text" value format may require translation for National/Regional procedures.

8.1. Qualifier MOL_TYPE
Definition In vivo molecule type of sequence
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
Value format free text
(Note: this value may require translation for National/Regional procedures)
Example <INSDQualifier_value>Heme (covalent)</INSDQualifier_value>
Comment The "NOTE" qualifier is mandatory for the feature keys: BINDING; CARBOHYD; CROSSLNK; DI SULFI Q; DNA_BI ND; DONN N; LI PI Q; METAL; MOD_RES; NP_BI ND and ZN_FING

8.3. Qualifier ORGANISM
Definition Scientific name of the organism that provided the peptide
Value format free text
(Note: this value may require translation for 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 5 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 trans_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 5.)

<table>
<thead>
<tr>
<th>Table 5: Genetic Code Tables</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1 - Standard Code</strong></td>
</tr>
<tr>
<td><strong>AA</strong> = FFLSSSSYY**CC*WLLLPPPPHQQRRII</td>
</tr>
<tr>
<td><strong>Starts</strong> = --------------------------------- M--------------- M------------</td>
</tr>
<tr>
<td><strong>Base1</strong> = ttttttttttttttttttttttttttttttt</td>
</tr>
<tr>
<td><strong>Base2</strong> = ttttttttttttttttttttttttttttttt</td>
</tr>
<tr>
<td><strong>Base3</strong> = ttttttttttttttttttttttttttttttt</td>
</tr>
<tr>
<td><strong>2 - Vertebrate Mitochondrial Code</strong></td>
</tr>
<tr>
<td><strong>AA</strong> = FFLSSSSYY**CCWLLLLPPPPHQQRRII</td>
</tr>
<tr>
<td><strong>Starts</strong> = --------------------------------- M--------------- M------------</td>
</tr>
<tr>
<td><strong>Base1</strong> = ttttttttttttttttttttttttttttttt</td>
</tr>
<tr>
<td><strong>Base2</strong> = ttttttttttttttttttttttttttttttt</td>
</tr>
<tr>
<td><strong>Base3</strong> = ttttttttttttttttttttttttttttttt</td>
</tr>
<tr>
<td><strong>3 - Yeast Mitochondrial Code</strong></td>
</tr>
<tr>
<td><strong>AA</strong> = FFLSSSSYY**CCWTTTTPPPPHHQQRRII</td>
</tr>
<tr>
<td><strong>Starts</strong> = --------------------------------- M--------------- M------------</td>
</tr>
<tr>
<td><strong>Base1</strong> = ttttttttttttttttttttttttttttttt</td>
</tr>
<tr>
<td><strong>Base2</strong> = ttttttttttttttttttttttttttttttt</td>
</tr>
<tr>
<td><strong>Base3</strong> = ttttttttttttttttttttttttttttttt</td>
</tr>
<tr>
<td><strong>4 - Mold, Protozoan, Coelenterate Mitochondrial Code &amp; Mycoplasma/Spiroplasma Code</strong></td>
</tr>
<tr>
<td><strong>AA</strong> = FFLSSSSYY**CCWLLLLPPPPHQQRRII</td>
</tr>
<tr>
<td><strong>Starts</strong> = --------------------------------- M--------------- M------------</td>
</tr>
<tr>
<td><strong>Base1</strong> = ttttttttttttttttttttttttttttttt</td>
</tr>
<tr>
<td><strong>Base2</strong> = ttttttttttttttttttttttttttttttt</td>
</tr>
<tr>
<td><strong>Base3</strong> = ttttttttttttttttttttttttttttttt</td>
</tr>
<tr>
<td><strong>5 - Invertebrate Mitochondrial Code</strong></td>
</tr>
<tr>
<td><strong>AA</strong> = FFLSSSSYY**CCWLLLLPPPPHQQRRII</td>
</tr>
<tr>
<td><strong>Starts</strong> = --------------------------------- M--------------- M------------</td>
</tr>
<tr>
<td><strong>Base1</strong> = ttttttttttttttttttttttttttttttt</td>
</tr>
<tr>
<td><strong>Base2</strong> = ttttttttttttttttttttttttttttttt</td>
</tr>
<tr>
<td><strong>Base3</strong> = ttttttttttttttttttttttttttttttt</td>
</tr>
<tr>
<td><strong>6 - Ciliate, Dasycladacean and Hexamita Nuclear Code</strong></td>
</tr>
<tr>
<td><strong>AA</strong> = FFLSSSSYYQCC*WLLLPPPPHQQRRII</td>
</tr>
<tr>
<td><strong>Starts</strong> = --------------------------------- M--------------- M------------</td>
</tr>
<tr>
<td><strong>Base1</strong> = ttttttttttttttttttttttttttttttt</td>
</tr>
<tr>
<td><strong>Base2</strong> = ttttttttttttttttttttttttttttttt</td>
</tr>
<tr>
<td><strong>Base3</strong> = ttttttttttttttttttttttttttttttt</td>
</tr>
</tbody>
</table>
9 - Echinoderm and Flatworm Mitochondrial Code

AAs = FFLSSSYY**CCWL LLLPPPHHQRRRII I MTTTNNKSSSSSVVVVAAAADDEE GGGG
Starts = ----------------------------------- M--------------- M------------
Base1 = tttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttt
### 21 - Trematode Mitochondrial Code

<table>
<thead>
<tr>
<th>AA5</th>
<th>FFLSSSSYY**CCWLLLPPPPHQQRRII</th>
<th>MTTTTNNKSSS5SVVVAAAAADDEEGGG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starts</td>
<td>----------------------------</td>
<td>M-------------------------------</td>
</tr>
</tbody>
</table>
| Base1 | tttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttttt
### 28 - Condylostoma Nuclear Code

<table>
<thead>
<tr>
<th>AAs</th>
<th>FFLLSSSSYYQCCWLLLLPPPHQQRRI</th>
<th>MTHTNNKKSRRVVVVAADDEEGGGG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starts</td>
<td>-----------------------------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>Base1</td>
<td>ttttttttttcccccccccMMMMMMMM</td>
<td></td>
</tr>
<tr>
<td>Base2</td>
<td>ttttccccaaaaggggtttccccaaaaggggtttccccaaaagggg</td>
<td></td>
</tr>
<tr>
<td>Base3</td>
<td>tcagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cag</td>
<td></td>
</tr>
</tbody>
</table>

### 29 - Mesodinium Nuclear Code

<table>
<thead>
<tr>
<th>AAs</th>
<th>FFLLSSSSYYYCCWLLLLPPPPHQQRRI</th>
<th>MTHTNNKKSRRVVVVAADDEEGGGG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starts</td>
<td>-----------------------------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>Base1</td>
<td>tttttttttttttcccccccccccccccc</td>
<td></td>
</tr>
<tr>
<td>Base2</td>
<td>ttttccccaaaaggggtttttccccaaaaggggtttttccccaaaagggg</td>
<td></td>
</tr>
<tr>
<td>Base3</td>
<td>tcagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cag</td>
<td></td>
</tr>
</tbody>
</table>

### 30 - Peritrich Nuclear Code

<table>
<thead>
<tr>
<th>AAs</th>
<th>FFLLSSSSYYECWWLLLLPPPPHHQRRRI</th>
<th>MTHTNNKKSRRVVVVAADDEEGGGG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starts</td>
<td>-----------------------------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>Base1</td>
<td>tttttttttttttttcccccccccccccccc</td>
<td></td>
</tr>
<tr>
<td>Base2</td>
<td>ttttccccaaaaggggttttccccaaaaggggttttccccaaaagggg</td>
<td></td>
</tr>
<tr>
<td>Base3</td>
<td>tcagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cag</td>
<td></td>
</tr>
</tbody>
</table>

### 31 - Blastocrithidia Nuclear Code

<table>
<thead>
<tr>
<th>AAs</th>
<th>FFLLSSSSYYECWWLLLLPPPPHHQRRRI</th>
<th>MTHTNNKKSRRVVVVAADDEEGGGG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starts</td>
<td>-----------------------------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>Base1</td>
<td>tttttttttttttttccccccccccccccc</td>
<td></td>
</tr>
<tr>
<td>Base2</td>
<td>ttttccccaaaaggggttttccccaaaaggggttttccccaaaagggg</td>
<td></td>
</tr>
<tr>
<td>Base3</td>
<td>tcagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cag</td>
<td></td>
</tr>
</tbody>
</table>

### 32 - Cephalodiscidae Mitochondrial UAA-Tyr Code

<table>
<thead>
<tr>
<th>AAs</th>
<th>FFLLSSSSYY*CCWLLLLPPPPHQQRRI</th>
<th>MTHTNNKKSRRVVVVAADDEEGGGG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starts</td>
<td>-----------------------------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>Base1</td>
<td>tttttttttttttttccccccccccccccc</td>
<td></td>
</tr>
<tr>
<td>Base2</td>
<td>ttttccccaaaaggggttttccccaaaaggggttttccccaaaagggg</td>
<td></td>
</tr>
<tr>
<td>Base3</td>
<td>tcagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cagt cag</td>
<td></td>
</tr>
</tbody>
</table>

[Annex II follows]
ANNEX II

DOCUMENT TYPE DEFINITION (DTD) FOR SEQUENCE LISTING

Version 1.2

Approved by the Committee on WIPO Standards (CWS)
at its sixt session on October 19, 2018

<?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 1.2//EN" "ST26SequenceListing_V1_2.dtd"
*******************************************************************************************
****
* PUBLIC DTD URL
* https://www.wipo.int/standards/dtd/ST26SequenceListing_V1_2.dtd
*******************************************************************************
Revision of Annex II to WIPO Standard ST.26 was approved by the Committee on WIPO Standards (CWS) at its sixth session.
*******************************************************************************
* CONTACTS
*******************************************************************************
xml.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
*******************************************************************************
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+)>
<!ATTLIST ST26SequenceListing
dtdVersion CDATA #REQUIRED
fileName CDATA #IMPLIED
softwareName CDATA #IMPLIED
softwareVersion CDATA #IMPLIED
productionDate 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
Application identification of the earliest claimed priority, which contains IPOfficeCode, ApplicationNumberText and FilingDate elements. For details, please see ApplicationIdentification.-->
<!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.-->
<!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).-->
<!ELEMENT InventorName (#PCDATA)>
<!ATTLIST InventorName
languageCode CDATA #REQUIRED
>
<!--InventorNameLatin

</!ELEMENT ST26SequenceListing>
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).

```xml
<!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.
-->
<!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)>
```

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 a 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)

[Annex III follows]
ANNEX III

SEQUENCE LISTING SPECIMEN (XML file)

Version 1.2

Approved by the Committee on WIPO Standards (CWS)
at its sixt session on October 19, 2018

The Annex III is available at: https://www.wipo.int/standards/en/docs/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 1.2

Approved by the Committee on WIPO Standards (CWS)
at its sixt session on October 19, 2018

The ampersand character (0026) is only permitted as part of a predefined entity or as part of a numeric character reference (&#xnnnn;). 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 value.

<table>
<thead>
<tr>
<th>Unicode code point</th>
<th>Character</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>0020</td>
<td>SPACE</td>
<td></td>
</tr>
<tr>
<td>0021</td>
<td>!</td>
<td>EXCLAMATION MARK</td>
</tr>
<tr>
<td>0022</td>
<td>&quot;</td>
<td>QUOTATION MARK</td>
</tr>
<tr>
<td>0023</td>
<td>#</td>
<td>NUMMER SIGN</td>
</tr>
<tr>
<td>0024</td>
<td>$</td>
<td>DOLLAR SIGN</td>
</tr>
<tr>
<td>0025</td>
<td>%</td>
<td>PERCENT SIGN</td>
</tr>
<tr>
<td>0026</td>
<td>&amp;</td>
<td>AMPERSAND</td>
</tr>
<tr>
<td>0027</td>
<td>'</td>
<td>APOSTROPE</td>
</tr>
<tr>
<td>0028</td>
<td>(</td>
<td>LEFT PARENTHESES</td>
</tr>
<tr>
<td>0029</td>
<td>)</td>
<td>RIGHT PARENTHESES</td>
</tr>
<tr>
<td>002A</td>
<td>+</td>
<td>PLUS SIGN</td>
</tr>
<tr>
<td>002B</td>
<td>,</td>
<td>COMMA</td>
</tr>
<tr>
<td>002D</td>
<td>-</td>
<td>HYPHEN-MINUS</td>
</tr>
<tr>
<td>002E</td>
<td>.</td>
<td>FULL STOP</td>
</tr>
<tr>
<td>002F</td>
<td>/</td>
<td>SOLIDUS</td>
</tr>
<tr>
<td>0030</td>
<td>0</td>
<td>DIGIT ZERO</td>
</tr>
<tr>
<td>0031</td>
<td>1</td>
<td>DIGIT ONE</td>
</tr>
<tr>
<td>0032</td>
<td>2</td>
<td>DIGIT TWO</td>
</tr>
<tr>
<td>0033</td>
<td>3</td>
<td>DIGIT THREE</td>
</tr>
<tr>
<td>0034</td>
<td>4</td>
<td>DIGIT FOUR</td>
</tr>
<tr>
<td>0035</td>
<td>5</td>
<td>DIGIT FIVE</td>
</tr>
<tr>
<td>0036</td>
<td>6</td>
<td>DIGIT SIX</td>
</tr>
<tr>
<td>0037</td>
<td>7</td>
<td>DIGIT SEVEN</td>
</tr>
<tr>
<td>0038</td>
<td>8</td>
<td>DIGIT EIGHT</td>
</tr>
<tr>
<td>0039</td>
<td>9</td>
<td>DIGIT NINE</td>
</tr>
<tr>
<td>003A</td>
<td>:</td>
<td>COLON</td>
</tr>
<tr>
<td>003B</td>
<td>;</td>
<td>SEMICOLON</td>
</tr>
<tr>
<td>003C</td>
<td>&lt;</td>
<td>LESS-THAN-SIGN</td>
</tr>
<tr>
<td>003D</td>
<td>=</td>
<td>EQUALS SIGN</td>
</tr>
<tr>
<td>003E</td>
<td>&gt;</td>
<td>GREATER-THAN-SIGN</td>
</tr>
<tr>
<td>003F</td>
<td>?</td>
<td>QUESTION MARK</td>
</tr>
<tr>
<td>0040</td>
<td>@</td>
<td>COMMERCIAL AT</td>
</tr>
<tr>
<td>0041</td>
<td>A</td>
<td>LATIN CAPITAL LETTER A</td>
</tr>
<tr>
<td>0042</td>
<td>B</td>
<td>LATIN CAPITAL LETTER B</td>
</tr>
<tr>
<td>0043</td>
<td>C</td>
<td>LATIN CAPITAL LETTER C</td>
</tr>
<tr>
<td>0044</td>
<td>D</td>
<td>LATIN CAPITAL LETTER D</td>
</tr>
<tr>
<td>0045</td>
<td>E</td>
<td>LATIN CAPITAL LETTER E</td>
</tr>
<tr>
<td>0046</td>
<td>F</td>
<td>LATIN CAPITAL LETTER F</td>
</tr>
<tr>
<td>0047</td>
<td>G</td>
<td>LATIN CAPITAL LETTER G</td>
</tr>
<tr>
<td>0048</td>
<td>H</td>
<td>LATIN CAPITAL LETTER H</td>
</tr>
<tr>
<td>0049</td>
<td>I</td>
<td>LATIN CAPITAL LETTER I</td>
</tr>
<tr>
<td>004A</td>
<td>J</td>
<td>LATIN CAPITAL LETTER J</td>
</tr>
<tr>
<td>Unicode code point</td>
<td>Character</td>
<td>Name</td>
</tr>
<tr>
<td>--------------------</td>
<td>-----------</td>
<td>---------------------------</td>
</tr>
<tr>
<td>004B</td>
<td>K</td>
<td>LATIN CAPITAL LETTER K</td>
</tr>
<tr>
<td>004C</td>
<td>L</td>
<td>LATIN CAPITAL LETTER L</td>
</tr>
<tr>
<td>004D</td>
<td>M</td>
<td>LATIN CAPITAL LETTER M</td>
</tr>
<tr>
<td>004E</td>
<td>N</td>
<td>LATIN CAPITAL LETTER N</td>
</tr>
<tr>
<td>004F</td>
<td>O</td>
<td>LATIN CAPITAL LETTER O</td>
</tr>
<tr>
<td>0050</td>
<td>P</td>
<td>LATIN CAPITAL LETTER P</td>
</tr>
<tr>
<td>0051</td>
<td>Q</td>
<td>LATIN CAPITAL LETTER Q</td>
</tr>
<tr>
<td>0052</td>
<td>R</td>
<td>LATIN CAPITAL LETTER R</td>
</tr>
<tr>
<td>0053</td>
<td>S</td>
<td>LATIN CAPITAL LETTER S</td>
</tr>
<tr>
<td>0054</td>
<td>T</td>
<td>LATIN CAPITAL LETTER T</td>
</tr>
<tr>
<td>0055</td>
<td>U</td>
<td>LATIN CAPITAL LETTER U</td>
</tr>
<tr>
<td>0056</td>
<td>V</td>
<td>LATIN CAPITAL LETTER V</td>
</tr>
<tr>
<td>0057</td>
<td>W</td>
<td>LATIN CAPITAL LETTER W</td>
</tr>
<tr>
<td>0058</td>
<td>X</td>
<td>LATIN CAPITAL LETTER X</td>
</tr>
<tr>
<td>0059</td>
<td>Y</td>
<td>LATIN CAPITAL LETTER Y</td>
</tr>
<tr>
<td>005A</td>
<td>Z</td>
<td>LATIN CAPITAL LETTER Z</td>
</tr>
<tr>
<td>005B</td>
<td>{</td>
<td>LEFT SQUARE Bracket</td>
</tr>
<tr>
<td>005C</td>
<td>}</td>
<td>RIGHT SQUARE Bracket</td>
</tr>
<tr>
<td>005D</td>
<td>^</td>
<td>CIRCUMFLEX ACCENT</td>
</tr>
<tr>
<td>005E</td>
<td>_</td>
<td>LOW LINE</td>
</tr>
<tr>
<td>005F</td>
<td>`</td>
<td>GRAVE ACCENT</td>
</tr>
<tr>
<td>0060</td>
<td>a</td>
<td>LATIN SMALL LETTER A</td>
</tr>
<tr>
<td>0061</td>
<td>b</td>
<td>LATIN SMALL LETTER B</td>
</tr>
<tr>
<td>0062</td>
<td>c</td>
<td>LATIN SMALL LETTER C</td>
</tr>
<tr>
<td>0063</td>
<td>d</td>
<td>LATIN SMALL LETTER D</td>
</tr>
<tr>
<td>0064</td>
<td>e</td>
<td>LATIN SMALL LETTER E</td>
</tr>
<tr>
<td>0065</td>
<td>f</td>
<td>LATIN SMALL LETTER F</td>
</tr>
<tr>
<td>0066</td>
<td>g</td>
<td>LATIN SMALL LETTER G</td>
</tr>
<tr>
<td>0067</td>
<td>h</td>
<td>LATIN SMALL LETTER H</td>
</tr>
<tr>
<td>0068</td>
<td>i</td>
<td>LATIN SMALL LETTER I</td>
</tr>
<tr>
<td>0069</td>
<td>j</td>
<td>LATIN SMALL LETTER J</td>
</tr>
<tr>
<td>006A</td>
<td>k</td>
<td>LATIN SMALL LETTER K</td>
</tr>
<tr>
<td>006B</td>
<td>l</td>
<td>LATIN SMALL LETTER L</td>
</tr>
<tr>
<td>006C</td>
<td>m</td>
<td>LATIN SMALL LETTER M</td>
</tr>
<tr>
<td>006D</td>
<td>n</td>
<td>LATIN SMALL LETTER N</td>
</tr>
<tr>
<td>006E</td>
<td>o</td>
<td>LATIN SMALL LETTER O</td>
</tr>
<tr>
<td>006F</td>
<td>p</td>
<td>LATIN SMALL LETTER P</td>
</tr>
<tr>
<td>0070</td>
<td>q</td>
<td>LATIN SMALL LETTER Q</td>
</tr>
<tr>
<td>0071</td>
<td>r</td>
<td>LATIN SMALL LETTER R</td>
</tr>
<tr>
<td>0072</td>
<td>s</td>
<td>LATIN SMALL LETTER S</td>
</tr>
<tr>
<td>0073</td>
<td>t</td>
<td>LATIN SMALL LETTER T</td>
</tr>
<tr>
<td>0074</td>
<td>u</td>
<td>LATIN SMALL LETTER U</td>
</tr>
<tr>
<td>0075</td>
<td>v</td>
<td>LATIN SMALL LETTER V</td>
</tr>
<tr>
<td>0076</td>
<td>w</td>
<td>LATIN SMALL LETTER W</td>
</tr>
<tr>
<td>0077</td>
<td>x</td>
<td>LATIN SMALL LETTER X</td>
</tr>
<tr>
<td>0078</td>
<td>y</td>
<td>LATIN SMALL LETTER Y</td>
</tr>
<tr>
<td>0079</td>
<td>z</td>
<td>LATIN SMALL LETTER Z</td>
</tr>
<tr>
<td>007A</td>
<td>(</td>
<td>LEFT CURLY BRACKET</td>
</tr>
<tr>
<td>007B</td>
<td>)</td>
<td>RIGHT CURLY BRACKET</td>
</tr>
<tr>
<td>007C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>007D</td>
<td>}</td>
<td>RIGHT CURLY BRACKET</td>
</tr>
<tr>
<td>007E</td>
<td>~</td>
<td>TILDE</td>
</tr>
</tbody>
</table>

[Annex V follows]
ANNEX V

ADDITIONAL DATA EXCHANGE REQUIREMENTS (FOR PATENT OFFICES ONLY)

Version 1.2

Approved by the Committee on WIPO Standards (CWS)
at its sixt session on October 19, 2018

In the context of data exchange with database providers (INSD members), 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 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

Version 1.3

Revision approved by the Committee on WIPO Standards (CWS)
at its seventh session on July 5, 2019

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 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 symbols or their upper case equivalents1) and the amino acid symbols set forth in Section 3, Table 3 of ST.26 Annex 1 (i.e. the upper case symbols or their lower case equivalents1). Symbols other than those set forth in these tables are "nonconventional".

A sequence is sometimes disclosed in a non-preferred manner by "enumeration of its residues" using conventional abbreviations or full names (as opposed to conventional symbols) as set forth in Tables A and B below, conventional symbols or abbreviations used in a nonconventional manner, nonconventional symbols or abbreviations, chemical formulas/structures, or shorthand formulas. Care should be taken to disclose sequences in the preferred manner; however, where sequences are disclosed in a non-preferred manner, consultation of the explanation of the sequence in the disclosure may be necessary to determine the meaning of the non-preferred symbol or abbreviation.

Where a conventional symbol or abbreviation 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. Otherwise, if the symbol is used in a nonconventional manner, the explanation is necessary to determine whether ST.26 paragraph 7 requires inclusion in the sequence listing or whether paragraph 8 prohibits inclusion.

Where a nonconventional symbol or abbreviation is disclosed as equivalent to a conventional symbol or abbreviation (e.g., "Z1" means "A"), or to a specific sequence of conventional symbols (e.g., "Z1" 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., "Z1" 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.

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".

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 "n" or "X" ambiguity symbols, "n" or "X" is construed to represent any nucleotide or amino acid, 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 which are represented by the most restrictive ambiguity symbols that include the most disclosed embodiments. However, inclusion of additional specific sequences is strongly encouraged where practical, e.g., which 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.

---

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).
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 “a”, “c”, “g”, or “t/u” except where it is used with a further description;

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

i. modified nucleotide, 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. “unknown” nucleotide, i.e., not determined, not disclosed, or unsure;

iii. an abasic site; or

d. 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;


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

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

ii. “unknown” amino acid, i.e., not determined, not disclosed, or unsure;

d. may be used to represent a sequence variant, i.e., alternatives, deletions, insertions, or substitutions, where “X” is the most restrictive ambiguity symbol.
### Table A – Conventional Nucleotide Symbols, Abbreviations, and Names

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Abbreviation</th>
<th>Nucleotide Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td></td>
<td>Adenine</td>
</tr>
<tr>
<td>c</td>
<td></td>
<td>Cytosine</td>
</tr>
<tr>
<td>g</td>
<td></td>
<td>Guanine</td>
</tr>
<tr>
<td>t</td>
<td>a or c</td>
<td>Thymine in DNA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Uracil in RNA (t/u)</td>
</tr>
<tr>
<td>m</td>
<td>a or c</td>
<td></td>
</tr>
<tr>
<td>r</td>
<td>a or g</td>
<td></td>
</tr>
<tr>
<td>w</td>
<td>a or t/u</td>
<td></td>
</tr>
<tr>
<td>s</td>
<td>c or g</td>
<td></td>
</tr>
<tr>
<td>y</td>
<td>c or t/u</td>
<td></td>
</tr>
<tr>
<td>k</td>
<td>g or t/u</td>
<td></td>
</tr>
<tr>
<td>v</td>
<td>a or c or g;</td>
<td>not t/u</td>
</tr>
<tr>
<td>h</td>
<td>a or c or t/u; not g</td>
<td></td>
</tr>
<tr>
<td>d</td>
<td>a or g or t/u; not c</td>
<td></td>
</tr>
<tr>
<td>b</td>
<td>c or g or t/u; not a</td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>a or c or g or t/u; “unknown” or “other”</td>
<td></td>
</tr>
</tbody>
</table>
### Table B – Conventional Amino Acid Symbols, Abbreviations, and Names

<table>
<thead>
<tr>
<th>Symbol</th>
<th>3-Letter Abbreviation</th>
<th>Amino Acid Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Ala</td>
<td>Alanine</td>
</tr>
<tr>
<td>R</td>
<td>Arg</td>
<td>Arginine</td>
</tr>
<tr>
<td>N</td>
<td>Asn</td>
<td>Asparagine</td>
</tr>
<tr>
<td>D</td>
<td>Asp</td>
<td>Aspartic Acid (Aspartate)</td>
</tr>
<tr>
<td>C</td>
<td>Cys</td>
<td>Cysteine</td>
</tr>
<tr>
<td>E</td>
<td>Glu</td>
<td>Glutamic Acid (Glutamate)</td>
</tr>
<tr>
<td>Q</td>
<td>Gin</td>
<td>Glutamine</td>
</tr>
<tr>
<td>G</td>
<td>Gly</td>
<td>Glycine</td>
</tr>
<tr>
<td>H</td>
<td>His</td>
<td>Histidine</td>
</tr>
<tr>
<td>I</td>
<td>Ile</td>
<td>Isoleucine</td>
</tr>
<tr>
<td>L</td>
<td>Leu</td>
<td>Leucine</td>
</tr>
<tr>
<td>K</td>
<td>Lys</td>
<td>Lysine</td>
</tr>
<tr>
<td>M</td>
<td>Met</td>
<td>Methionine</td>
</tr>
<tr>
<td>F</td>
<td>Phe</td>
<td>Phenylalanine</td>
</tr>
<tr>
<td>P</td>
<td>Pro</td>
<td>Proline</td>
</tr>
<tr>
<td>O</td>
<td>Pyl</td>
<td>Pyrolysine</td>
</tr>
<tr>
<td>S</td>
<td>Ser</td>
<td>Serine</td>
</tr>
<tr>
<td>U</td>
<td>Sec</td>
<td>Selenocysteine</td>
</tr>
<tr>
<td>T</td>
<td>Thr</td>
<td>Threonine</td>
</tr>
<tr>
<td>W</td>
<td>Trp</td>
<td>Tryptophan</td>
</tr>
<tr>
<td>Y</td>
<td>Tyr</td>
<td>Tyrosine</td>
</tr>
<tr>
<td>V</td>
<td>Val</td>
<td>Valine</td>
</tr>
<tr>
<td>B</td>
<td>Asx</td>
<td>Aspartic acid or Asparagine</td>
</tr>
<tr>
<td>Z</td>
<td>Gix</td>
<td>Glutamine or Glutamic Acid</td>
</tr>
<tr>
<td>J</td>
<td>Xle</td>
<td>Leucine or Isoleucine</td>
</tr>
<tr>
<td>X</td>
<td>Xaa</td>
<td>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”</td>
</tr>
</tbody>
</table>
### EXAMPLE INDEX

#### Paragraph 3(a) – Definition of “amino acid”

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

**Cross-referenced examples**
- Example 29-1: Most restrictive ambiguity symbol for an “other” amino acid
- Example 30-1: Feature key “CARBOHYD”

#### Paragraph 3(c) – Definition of “enumeration of its residues”

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

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

**Cross-referenced examples**
- Example 27-1: Shorthand formula for a nucleotide sequence
- Example 27-3: Shorthand formula - four or more specifically defined amino acids

#### Paragraph 3(f) – Definition of “modified nucleotide”

**Cross-referenced examples**
- Example 3(g)-4: Nucleic Acid Analogues

#### Paragraph 3(g) – Definition of “nucleotide”

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

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

**Example 3(g)-3**: Abasic site

**Example 3(g)-4**: Nucleic Acid Analogues

**Cross-referenced examples**
- Example 11(b)-1: Double-stranded nucleotide sequence – different lengths
- Example 14-1: The symbol “t” represents uracil in RNA

#### Paragraph 3(k) – Definition of “specifically defined”

**Example 3(k)-1**: Nucleotide ambiguity symbols

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

**Example 3(k)-3**: Ambiguity symbol “n” used in a nonconventional manner

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

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

#### Paragraph 7 – Sequences for which inclusion in a sequence listing is required

**Cross-referenced examples**
- Example 28-1: Encoding nucleotide sequence and encoded amino acid sequence
Example 55-1: Combined DNA/RNA Molecule ......................................................................................... 61
Example 87-2: Feature location extends beyond the disclosed sequence .................................................. 63
Example 90-1: Amino acid sequence encoded by a coding sequence with introns .................................. 65

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

Example 7(a)-1: Branched nucleotide sequence ......................................................................................... 28
Example 7(a)-2: Linear nucleotide sequence having a secondary structure ................................................ 30
Example 7(a)-3: Nucleotide ambiguity symbols used in a nonconventional manner ................................ 31
Example 7(a)-4: Nucleotide ambiguity symbols used in a nonconventional manner ................................ 32
Example 7(a)-5: Nonconventional nucleotide symbols ............................................................................... 33
Example 7(a)-6: Nonconventional nucleotide symbols ............................................................................... 34

Cross-referenced examples

Example 3(g)-1: Nucleotide sequence interrupted by a C3 spacer ........................................................... 19
Example 3(g)-2: Nucleotide sequence with residue alternatives, including a C3 spacer .......................... 20
Example 3(g)-3: Abasic site .................................................................................................................. 21
Example 3(g)-4: Nucleic Acid Analogues ............................................................................................... 22
Example 3(k)-1: Nucleotide ambiguity symbols ....................................................................................... 23
Example 3(k)-2: Ambiguity symbol "n" used in both a conventional and nonconventional manner .......... 24
Example 3(k)-3: Ambiguity symbol "n" used in a nonconventional manner ................................................ 25
Example 3(k)-4: Ambiguity symbols other than "n" are "specifically defined" .............................................. 26
Example 11(a)-1: Double-stranded nucleotide sequence – same lengths .............................................. 44
Example 11(b)-1: Double-stranded nucleotide sequence – different lengths ........................................... 45
Example 11(b)-2: Double-stranded nucleotide sequence – no base-pairing segment ............................. 46
Example 14-1: The symbol "t" represents uracil in RNA ............................................................................ 47
Example 87-1: Encoding nucleotide sequence and encoded amino acid sequence ................................ 62
Example 91-1: Representation of enumerated variants ............................................................................. 67
Example 93(b)-1: Representation of individual variant sequences with multiple interdependent variations ........................................................................................................................................... 72

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

Example 7(b)-1: Four or more specifically defined amino acids .................................................................... 35
Example 7(b)-2: Branched amino acid sequence ....................................................................................... 36
Example 7(b)-3: Branched amino acid sequence ....................................................................................... 39
Example 7(b)-4: Cyclic peptide containing a branched amino acid sequence ............................................ 40
Example 7(b)-5: Cyclic peptide containing a branched amino acid sequence

Cross-referenced examples

Example 3(a)-1: D-amino acids .......................................................... 16
Example 3(c)-1: Enumeration of amino acids by chemical structure ......................................................... 17
Example 3(c)-2: Shorthand formula for an amino acid sequence ................................................................. 18
Example 3(k)-5: Ambiguity abbreviation “Xaa” used in a nonconventional manner .............................. 27
Example 27-1: Shorthand formula for a nucleotide sequence ................................................................. 49
Example 27-3: Shorthand formula - four or more specifically defined amino acids .................................. 51
Example 29-1: Most restrictive ambiguity symbol for an “other” amino acid ........................................ 54
Example 30-1: Feature key “CARBODHYD” .............................................................................................. 55
Example 36-1: Sequence with a region of a known number of “X” residues represented as a single sequence .......................................................... 56
Example 37-1: Sequence with regions of an unknown number of “X” residues must not be represented as a single sequence .......................................................... 59
Example 37-2: Sequence with regions of an unknown number of “X” residues must not be represented as a single sequence .......................................................... 60
Example 87-1: Encoding nucleotide sequence and encoded amino acid sequence ................................ 62
Example 91-2: Representation of enumerated variants .............................................................................. 68
Example 91-3: Representation of a consensus sequence ............................................................................. 69
Example 92-1: Representation of single sequence with enumerated alternative amino acids .................. 70
Example 93(a)-1: Representation of a variant sequence by annotation of the primary sequence ............ 71

Paragraph 8 – Threshold for inclusion of sequences

Cross-referenced examples

Example 3(k)-1: Nucleotide ambiguity symbols ...................................................................................... 23
Example 3(k)-2: Ambiguity symbol “n” used in both a conventional and nonconventional manner ......... 24
Example 7(a)-1: Branched nucleotide sequence ......................................................................................... 28
Example 7(a)-6: Nonconventional nucleotide symbols ............................................................................. 34
Example 7(b)-1: Four or more specifically defined amino acids ............................................................ 35
Example 7(b)-2: Branched amino acid sequence ....................................................................................... 36
Example 7(b)-4: Cyclic peptide containing a branched amino acid sequence .................................... 40
Example 14-1: The symbol “t” represents uracil in RNA ........................................................................ 47
Example 37-1: Sequence with regions of an unknown number of “X” residues must not be represented as a single sequence .......................................................... 59
Example 37-2: Sequence with regions of an unknown number of “X” residues must not be represented as a single sequence .......................................................... 60
Example 92-1: Representation of single sequence with enumerated alternative amino acids

Paragraph 11 – Representation of a nucleotide sequence

Cross-referenced examples
Example 3(g)-4: Nucleic Acid Analogues
Example 7(a)-1: Branched nucleotide sequence

Paragraph 11(a) – Double-stranded nucleotide sequence - fully complementary

Example 11(a)-1: Double-stranded nucleotide sequence – same lengths

Paragraph 11(b) – Double-stranded nucleotide sequence – not fully complementary

Example 11(b)-1: Double-stranded nucleotide sequence – different lengths
Example 11(b)-2: Double-stranded nucleotide sequence – no base-pairing segment

Paragraph 13 – Representation of nucleotides

Cross-referenced examples
Example 3(k)-2: Ambiguity symbol “n” used in both a conventional and nonconventional manner
Example 7(a)-1: Branched nucleotide sequence
Example 14-1: The symbol “t” represents uracil in RNA
Example 91-1: Representation of enumerated variants

Paragraph 14 – Symbol “t” construed as uracil in RNA

Example 14-1: The symbol “t” represents uracil in RNA

Cross-referenced examples
Example 55-1: Combined DNA/RNA Molecule

Paragraph 15 – The most restrictive nucleotide ambiguity symbol should be used

Cross-referenced examples
Example 3(g)-1: Nucleotide sequence interrupted by a C3 spacer
Example 3(g)-2: Nucleotide sequence with residue alternatives, including a C3 spacer
Example 3(k)-4: Ambiguity symbols other than “n” are “specifically defined”
Example 93(b)-1: Representation of individual variant sequences with multiple interdependent variations

Paragraph 16 – Representation of a modified amino acid

Cross-referenced examples
Example 3(g)-1: Nucleotide sequence interrupted by a C3 spacer
Example 3(g)-4: Nucleic Acid Analogues

Paragraph 17 – Annotation of a modified amino acid

Cross-referenced examples
Example 3(g)-1: Nucleotide sequence interrupted by a C3 spacer
Example 3(g)-3: Abasic site ....................................................................................................................... 21
Example 7(a)-1: Branched nucleotide sequence...................................................................................... 28
Example 7(a)-2: Linear nucleotide sequence having a secondary structure...................................... 30
Example 7(a)-6: Nonconventional nucleotide symbols........................................................................... 34

Paragraph 18 – Annotation of regions of consecutive modified nucleotides

Cross-referenced examples
Example 3(g)-4: Nucleic Acid Analogues ...................................................................................................... 22
Example 11(b)-1: Double-stranded nucleotide sequence – different lengths........................................ 45

Paragraph 19 – Annotation of uracil in DNA or thymine in RNA

Cross-referenced examples
Example 14-1: The symbol “t” represents uracil in RNA........................................................................ 47

Paragraph 25 – Amino acid sequence residue position number 1

Cross-referenced examples
Example 3(a)-1: D-amino acids..................................................................................................................... 16
Example 7(b)-4: Cyclic peptide containing a branched amino acid sequence........................................ 40
Example 7(b)-5: Cyclic peptide containing a branched amino acid sequence........................................ 43
Example 29-1: Most restrictive ambiguity symbol for an “other” amino acid........................................ 54

Paragraph 26 – Representation of amino acids

Cross-referenced examples
Example 7(b)-2: Branched amino acid sequence........................................................................................ 36
Example 7(b)-4: Cyclic peptide containing a branched amino acid sequence........................................ 40
Example 7(b)-5: Cyclic peptide containing a branched amino acid sequence........................................ 43
Example 36-1: Sequence with a region of a known number of “X” residues represented as a single sequence ............................................................................................................. 56
Example 87-1: Encoding nucleotide sequence and encoded amino acid sequence.................................. 62
Example 90-1: Amino acid sequence encoded by a coding sequence with introns.................................. 65
Example 91-2: Representation of enumerated variants ................................................................................ 68
Example 91-3: Representation of a consensus sequence ............................................................................ 69

Paragraph 27 – The most restrictive amino acid ambiguity symbol should be used

Example 27-1: Shorthand formula for a nucleotide sequence........................................................................ 49
Example 27-2: Shorthand formula - less than four specifically defined amino acids ............................. 50
Example 27-3: Shorthand formula - four or more specifically defined amino acids .................................. 51
Cross-referenced examples

Example 3(c)-2: Shorthand formula for an amino acid sequence.......................................................... 18
Example 7(b)-1: Four or more specifically defined amino acids .............................................................. 35
Example 29-1: Most restrictive ambiguity symbol for an “other” amino acid ........................................ 54
Example 36-1: Sequence with a region of a known number of “X” residues represented as a single sequence ................................................................. 56
Example 36-2: Sequence with multiple regions of a known number or range of “X” residues represented as a single sequence .................................................................................. 57
Example 36-3: Sequence with multiple regions of a known number or range of “X” residues represented as a single sequence .................................................................................. 58
Example 37-2: Sequence with regions of an unknown number of “X” residues must not be represented as a single sequence ................................................................. 60
Example 91-3: Representation of a consensus sequence ........................................................................... 69
Example 92-1: Representation of single sequence with enumerated alternative amino acids ...................... 70
Example 93(a)-1: Representation of a variant sequence by annotation of the primary sequence ............... 71

Paragraph 28 – Amino acid sequences separated by internal terminator symbols

Example 28-1: Encoding nucleotide sequence and encoded amino acid sequence .......................................... 52

Cross-referenced examples

Example 87-1: Encoding nucleotide sequence and encoded amino acid sequence ...................................... 62
Example 90-1: Amino acid sequence encoded by a coding sequence with introns ....................................... 65

Paragraph 29 – Representation of an “other” modified amino acid

Example 29-1: Most restrictive ambiguity symbol for an “other” amino acid ............................................. 54

Cross-referenced examples

Example 3(a)-1: D-amino acids.................................................................................................................. 16
Example 7(b)-2: Branched amino acid sequence......................................................................................... 36
Example 7(b)-3: Branched amino acid sequence......................................................................................... 39
Example 7(b)-4: Cyclic peptide containing a branched amino acid sequence ........................................... 40
Example 30-1: Feature key “CARBODHYD”.............................................................................................. 55

Paragraph 30 – Annotation of a modified amino acids

Example 30-1: Feature key “CARBODHYD” ............................................................................................. 55

Cross-referenced examples

Example 3(a)-1: D-amino acids.................................................................................................................. 16
Example 3(c)-1: Enumeration of amino acids by chemical structure ............................................................ 17
Example 7(b)-2: Branched amino acid sequence......................................................................................... 36
Example 7(b)-3: Branched amino acid sequence ................................................................. 39
Example 7(b)-4: Cyclic peptide containing a branched amino acid sequence .................... 40
Example 7(b)-5: Cyclic peptide containing a branched amino acid sequence .................... 43
Example 29-1: Most restrictive ambiguity symbol for an “other” amino acid .................... 54

Paragraph 31 – Representation of a D-amino acid

Cross-referenced examples
Example 3(a)-1: D-amino acids .......................................................................................... 16
Example 3(c)-1: Enumeration of amino acids by chemical structure ................................... 17
Example 7(b)-2: Branched amino acid sequence ................................................................. 36
Example 7(b)-3: Branched amino acid sequence ................................................................. 39
Example 7(b)-4: Cyclic peptide containing a branched amino acid sequence .................... 40
Example 7(b)-5: Cyclic peptide containing a branched amino acid sequence .................... 43

Paragraph 32 – Annotation of an “unknown” amino acid

Cross-referenced examples
Example 3(c)-1: Enumeration of amino acids by chemical structure ................................... 17

Paragraph 34 – Annotation of a contiguous region of “X” residues

Cross-referenced examples
Example 29-1: Most restrictive ambiguity symbol for an “other” amino acid .................... 54

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 ................................................................. 56
Example 36-2: Sequence with multiple regions of a known number or range of “X” residues represented as a single sequence ................................................................. 57
Example 36-3: Sequence with multiple regions of a known number or range of “X” residues represented as a single sequence ................................................................. 58

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 ................................................................. 59
Example 37-2: Sequence with regions of an unknown number of “X” residues must not be represented as a single sequence ................................................................. 60

Paragraph 41 – Reserved characters

Cross-referenced examples
Example 87-2: Feature location extends beyond the disclosed sequence ................................ 63
Paragraph 54 – The element INSDSeq_moltype

Cross-referenced examples
Example 14-1: The symbol “t” represents uracil in RNA ................................................................. 47

Paragraph 55 – A nucleotide sequence that contains both DNA and RNA segments

Example 55-1: Combined DNA/RNA Molecule ..................................................................................... 61

Paragraph 56 – Example illustrating a nucleotide sequence that contains both DNA and RNA segments

Cross-referenced examples
Example 55-1: Combined DNA/RNA Molecule ..................................................................................... 61

Paragraph 57 – The element INSDSeq_sequence

Cross-referenced examples
Example 28-1: Encoding nucleotide sequence and encoded amino acid sequence ................................. 52
Example 90-1: Amino acid sequence encoded by a coding sequence with introns ........................................ 65

Paragraph 65 – Location descriptor

Cross-referenced examples
Example 3(g)-4: Nucleic Acid Analogues ................................................................................................. 22
Example 87-2: Feature location extends beyond the disclosed sequence .................................................. 63

Paragraph 66 – Location descriptor syntax

Cross-referenced examples
Example 3(g)-4: Nucleic Acid Analogues ................................................................................................. 22
Example 29-1: Most restrictive ambiguity symbol for an “other” amino acid ............................................. 54
Example 87-2: Feature location extends beyond the disclosed sequence .................................................. 63

Paragraph 67 – Location operator

Cross-referenced examples
Example 7(b)-4: Cyclic peptide containing a branched amino acid sequence ........................................... 40

Paragraph 68 – Join and order location operators

Cross-referenced examples
Example 7(b)-4: Cyclic peptide containing a branched amino acid sequence ........................................... 40

Paragraph 70 – Feature locations

Cross-referenced examples
Example 29-1: Most restrictive ambiguity symbol for an “other” amino acid ............................................. 54
Example 87-2: Feature location extends beyond the disclosed sequence .................................................. 63

Paragraph 71 – Representation of the characters “<” and “>” in a location descriptor

Cross-referenced examples
Example 29-1: Most restrictive ambiguity symbol for an “other” amino acid .................................................. 54
Example 87-2: Feature location extends beyond the disclosed sequence ....................................................... 63

Paragraph 83 – Example illustrating a nucleotide sequence that is not naturally occurring

Cross-referenced examples

Example 55-1: Combined DNA/RNA Molecule ............................................................................................. 61

Paragraph 87 – “CDS” Feature key

Example 87-1: Encoding nucleotide sequence and encoded amino acid sequence .................................................... 62
Example 87-2: Feature location extends beyond the disclosed sequence ....................................................... 63

Cross-referenced examples

Example 90-1: Amino acid sequence encoded by a coding sequence with introns ............................................. 65

Paragraph 88 – The qualifiers “transl_table” and “translation”

Cross-referenced examples

Example 28-1: Encoding nucleotide sequence and encoded amino acid sequence ..................................... 52
Example 87-1: Encoding nucleotide sequence and encoded amino acid sequence ..................................... 62
Example 90-1: Amino acid sequence encoded by a coding sequence with introns ............................................. 65

Paragraph 90 – Encoded amino acid sequence inclusion in a sequence listing

Example 90-1: Amino acid sequence encoded by a coding sequence with introns ............................................. 65

Cross-referenced examples

Example 28-1: Encoding nucleotide sequence and encoded amino acid sequence ..................................... 52
Example 87-1: Encoding nucleotide sequence and encoded amino acid sequence ..................................... 62
Example 87-2: Feature location extends beyond the disclosed sequence ....................................................... 63

Paragraph 91 – Primary sequence and a variant each enumerated by its residue

Example 91-1: Representation of enumerated variants .......................................................................................... 67
Example 91-2: Representation of enumerated variants .......................................................................................... 68
Example 91-3: Representation of a consensus sequence .......................................................................................... 69

Paragraph 92 – Variant sequence disclosed as a single sequence with enumerated alternative residues

Example 92-1: Representation of single sequence with enumerated alternative amino acids ............................................ 70

Paragraph 93(a) – A variant sequence disclosed only by reference to a primary sequence with multiple independent variations

Example 93(a)-1: Representation of a variant sequence by annotation of the primary sequence ............................... 71

Paragraph 93(b) – A variant sequence disclosed only by reference to a primary sequence with multiple interdependent variations
Example 93(b)-1: Representation of individual variant sequences with multiple interdependent variations ............. 72

Paragraph 94 – Feature keys and qualifiers for a variant sequence

Cross-referenced examples

Example 29-1: Most restrictive ambiguity symbol for an “other” amino acid .................................................. 54

Example 91-3: Representation of a consensus sequence ............................................................................ 69

Example 92-1: Representation of single sequence with enumerated alternative amino acids ....................... 70

Paragraph 95– Annotation of a variant sequence

Cross-referenced examples

Example 29-1: Most restrictive ambiguity symbol for an “other” amino acid .................................................. 54

Example 91-3: Representation of a consensus sequence ............................................................................ 69

Example 92-1: Representation of single sequence with enumerated alternative amino acids ....................... 70
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 amino acids that are specifically defined (D-Ala, D-Glu, Lys, Gly, and D-Met). 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?

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 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
Paragraph 3(c) – Definition of “enumeration of its residues”

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

![Chemical structure](image)

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 be represented as:

VAFXGK (SEQ ID NO: 2)

wherein “X” represents an “other” modified amino acid: , 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-y1)-5-oxoheptanoic acid”. Further, additional feature keys “SITE” and qualifier “NOTE” are required to indicate the acetylation of the N-terminus and the methylation of the C-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” is required to indicate the acetylation of the N-terminus.

Relevant ST.26 paragraph(s): 3(c), 7(b), 29, 30, and 31
Example 3(c)-2: Shorthand formula for an amino acid sequence

$$(G\alpha z)_n$$

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 “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)

preferably annotated with the feature key REGION, feature location “&gt;5” (corresponds to &gt;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 “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, if “X” is intended to represent “any amino acid”, then it should 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:

\[ \text{Structure of C3 spacer} \]

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)
- cgccatgcatgc (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:

atgcatgcatgcatgcncggcatgcatgc

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

![Structure of C3 spacer](image)

**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:

atgcatgcatgcatgcvcggcatgcatgc (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)(b).

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:

\[ \text{PO}_4 - \text{tagttcattgactaaggctccccattgact-} \text{OH} \]

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 nucleotides according to ST.26 paragraph 3(g)(i)(2). 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:

\[ \text{tagttcattgactaaggctccccattgact} \] (SEQ ID NO: 11)

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, 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(d), 3(g), 7(a), 11, 16, 18, 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

According to paragraph 8, “A sequence listing must not 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.

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 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

The sequence “AATGCCGGAN” must not be included in a sequence listing.

However, a described alternative sequence may be included in a sequence listing if the “N” is replaced with a specifically defined nucleotide.

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

Inclusion of 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 three of the above sequences are included, 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 feature key “misc_difference” with feature location “10” should be used together with two “replace” qualifiers where the value for one would be “g” and the second would be “c”.

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(k), 7(a), 8, and 13
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 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, if “X” is intended to represent “any amino acid” in position 1, then it should 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:

\[ 3' \text{-CA(pnp)CACAC(pnp)CACAC(pnp)CACAC}{(5')}\text{NH}--\text{C(=O)CH}_23' \]

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

3'-CA(pnp)CACAC(pnp)CACAC(pnp)CACAC-(5')NH--C(=O)CH\(_2\)3' is segment A;

SP(O-)\((=O)\)CACACAAAAAAAAAAAAAAAAAAAAAAAAAAAAA 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

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**

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

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:

```
cacacaaaaaaaaaaaaaaaaaaaaaaaaa (SEQ ID NO: 18)
```

The first “c” in the sequence should be further described as a modified nucleotide 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 as a modified nucleotide 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.”

**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 \( \Psi \) 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 "\( \Psi \)" is equivalent to pseudouridine. The only conventional symbol that can be used to represent pseudouridine is "\( \text{n} \)"; therefore, the "\( \Psi \)" is a nonconventional symbol used to represent the conventional symbol "\( \text{n} \)" (see Introduction to this document). Accordingly, the sequence must be interpreted to have two "\( \text{n} \)" symbols in place of the two "\( \Psi \)" symbols.

The symbol "\( \text{u} \)" must not be used to represent uracil in an RNA molecule in the sequence listing. According to paragraph 14, the symbol "\( \text{t} \)" will be construed as uracil in RNA. The sequence must be included as:

gcggatttagctcagctggagagcgccagactgaatanctggagtcctgtgtncgatccacagaattcgcacca (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 "\( \text{n} \)" 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:

gatcattttttatattttttatattttttatattttttatgtac (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:

atctacgctatacgcatacgcatacgcatacgcatacgcatacgcatacgcactgtac (SEQ ID NO: 22)

Relevant ST.26 paragraphs: 7(a) and 13
Example 7(a)-5: Nonconventional nucleotide symbols

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' ATACGC ACT 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' ATACGC ACT 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-ATACGC ACT-ATACGC ACT-ATACGC ACT-ATACGC ACT-ATACGC ACT-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:

gatcatacgcactatacgcactatacgcactatacgcactatacgcactgtac (SEQ ID NO: 23)

Relevant ST.26 paragraphs: 7(a) and 13
Example 7(a)-6: Nonconventional nucleotide symbols

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 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

The enumerated sequence, 5' GATC-N-N-N-N-GTAC 3' must not 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?

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

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

XXXXXXXXDXXXXXXXXXXFXXXXXXXXXXXXXXXXXXXXXXXXXXXXAXXXXXXXXXXXXXXXXXXXGXXXXX

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:

XXXXXXXXDXXXXXXXXXXFXXXXXXXXXXXXXXXXXXXXXXXXXXXXAXXXXXXXXXXXXXXXXXXXGXXXXX

(SEQ ID NO: 25)

According to paragraph 27, “X” will be construed as any one of “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, if “X” is intended to represent “any amino acid”, then it should 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

The application describes a branched sequence where the 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-bonding. The peptide is illustrated as follows:

\[
\begin{align*}
\text{NH}_2 & \quad \text{ARG} \quad \text{ILE} \quad \text{SER} \quad \text{LEU} \\
\text{LYS} & \\
\text{NH}_2 & \quad \text{LEU} \quad \text{LEU} \\
\text{NH}_2 & \quad \text{TYR} \quad \text{PHE} \quad \text{ALA} \\
\text{LYS} & \\
\text{NH}_2 & \quad \text{LEU} \quad \text{LEU} \\
\text{LYS} & \\
\text{NH}_2 & \quad \text{ILE} \quad \text{PRO} \quad \text{ALA} \quad \text{CYS} \quad \text{THR} \quad \text{ALA} \\
\text{LYS} & \\
\text{NH}_2 & \quad \text{PHE} \quad \text{ARG} \quad \text{ALA} \quad \text{GLY} \\
\text{LYS} & \\
\text{NH}_2 & \quad \text{HIS} \quad \text{GLN} \quad \text{TYR} \quad \text{PHE} \quad \text{ALA} \\
\text{LYS} & \\
\text{NH}_2 & \quad \text{ALA} \quad \text{THR} \quad \text{PHE} \quad \text{GLY} \\
\text{LYS} & \\
\text{LYS} & \\
\text{Lys} & \quad \text{Ala-} \text{OH}
\end{align*}
\]

In the above branched peptide, the bonds between lysine and another amino acid depicted by \(\text{---}\) represent an amide linkage between the terminal amine of the lysine and the carboxyl end of the bonded amino acid. The bonds depicted by \(\text{\wedge\wedge\wedge\wedge}\) represent an amide linkage between the side chain amine of the lysine and the carboxyl end 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. Paragraph 7(b) requires that the unbranched or linear region of the sequence, containing four or more specifically defined amino acids, 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 circled.
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

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

The peptides YFA and LLK each contain only three specifically defined amino acids and therefore, they must not be included in the sequence listing as separate sequences with their own sequence identification numbers.
Question 3: How should the sequence(s) be represented in the sequence listing?

Peptides 1-6 must be represented with separate sequence identifiers:

- 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)

The cross linkage is preferably noted 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 29, 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. Preferably, 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”.

Relevant ST.26 paragraph(s): 7(b), 8, 26, 29, 30, and 31
Example 7(b)-3: Branched amino acid sequence

Peptide of the following sequence:

\[
\begin{align*}
\text{NH}_2 & \text{ASP-GLY-SER-ALA-LYS-LYS-LYS-lys-CO}_2 \text{H} \\
\text{NH}_2 & \text{ALA-ALA-SER-HIS-GLY}
\end{align*}
\]

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 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:

\[
\begin{align*}
\text{1.} & \text{ NH}_2 \text{ASP-GLY-SER-ALA-LYS-LYS-LYS-lys-CO}_2 \text{H} \\
\text{2.} & \text{ NH}_2 \text{ALA-ALA-SER-HIS-GLY}
\end{align*}
\]

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?

Sequences 1 and 2 must be represented with separate sequence identifiers:

- 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. Preferably 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

A patent application discloses the following structure:

The Cysteine and Leucine in the cyclic structure are linked through the side chain of the Cys and carbonyl 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 carbonyl terminus of the Leu are involved in the cyclization, the N-terminus of the cyclic peptide is located at Cys-1.

YES – the cyclic portion 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 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 in the sequence listing.

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

NO

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

The tripeptide branch contains only three specifically defined amino acids and therefore, it must not 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?

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 occurs through the side chain of cysteine (Cys) and the carboxyl terminus of the Leucine (Leu), the cysteine must be assigned position number 1 within the cyclic region of the peptide. Accordingly, the sequence must be represented as:

CALRDKL (SEQ ID NO: 89).

As indicated in the figure above, the amino acid sequence is cyclized through a thioester conjugation between the cysteine side chain and the carboxy terminus of the leucine. The feature key “SITE” must be used to describe the modified cysteine, which forms the intrachain linkage with leucine. The location operator join should be used with location descriptors to indicate the residues involved in the linkage, i.e. “join(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 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 side chain links the tripeptide ALE.

Relevant ST.26 paragraphs: 7(b), 8, 25, 26, 29, 30, 31, 67, and 68
Example 7(b)-5: Cyclic peptide containing a branched amino acid sequence

A patent application discloses the following branched cyclic peptide:

```
Leu—Arg—Asp—Gln—Ser
   |   |   |   |
Ala—Leu—Phe—Lys—Asn—Gly
```

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 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:

1. ---->

```
Leu—Arg—Asp—Gln—Ser
```

2. ---->

```
Ala—Leu—Phe—Lys—Asn—Gly
```

ST.26 requires inclusion of sequences 1 and 2 of this cyclic branched peptide in a sequence listing, each with their 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: 90)
```

Preferably, the sequence is 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 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. Accordingly, the sequence may be represented as:

```
ALFKNG  (SEQ. ID. NO: 91)
```

Alternatively, any other amino acid in the sequence could be designated as residue position number 1. The sequence ALFKNG 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’ -CCGTTAACGCTA-5’

5’ -GGCCAATTGCAGA-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

ggccacattgcgat (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'  
__________________________  
gggttaactgantccgc

The human gene ABC1 promoter region (top strand) bound by a 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 nucleotides according to ST.26 paragraph 3(g). Therefore, the 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:

cgcctnaagtcaatggg (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”. 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 nucleotides, such as “N-(2-aminoethyl) glycine nucleosides”.

The “n” residue must be further 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: “N-(2-aminoethyl) glycine 5-nitroindole or N-(2-aminoethyl) glycine 3-nitroindole”.

Relevant ST.26 paragraphs: 3(g), 7(a), 11(b), 17, and 18
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:

atcggatgcatatcattgattggcc (top strand) (SEQ ID NO: 38)

and

ggccaatatgtgctgatcccgat (bottom strand) (SEQ ID NO: 39)

Relevant ST.26 paragraphs: 7(a), 11(b), and 13
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:

```
segment A: ccugucgt-3'  
      Oh  
    N  
  CO  
O-P-O

segment B: uaguuguagggccgucccct-5' 
       OH  
    n - 3
```

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:

```
  O-N  
H-C  
O-P-O
```

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 8 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

Segment A contains fewer than 10 specifically defined nucleotides, and as per ST.26 paragraph 8, it must not be included in a sequence listing.
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. Accordingly, segment B must be included in the sequence listing as:

```
tcctgtcggagatgttgat (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. 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’ oxygen of the thymidine is attached through the linker (4-(3-hydroxybenzamido)butyl) phosphinic acid to another nucleotide sequence.” Where practicable, the other sequence may be directly indicated as the value in the qualifier “note”.

**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 a nucleotide 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.

Therefore, “\(z\)” is equivalent to the conventional symbol “\(X\)”, and the peptide in the example has eight enumerated amino acids, six of which are specifically defined glycine residues. 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 “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, if “\(X\)” is intended to represent “any amino acid”, then it should 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, the example does not disclose that “\(z\)” is the same amino acid in both positions in the expanded sequence. However, if “\(z\)” is disclosed as the same amino acid in both positions, then a feature key “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-Gly-Gly-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, 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

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?

A sequence containing 100 copies of GGGX is preferred (SEQ ID NO: 42). A further annotation should indicate that up to 98 copies of GGGX could be deleted. Inclusion of further 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 "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, if "X" is intended to represent "any amino acid", then it should 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), 26, and 27
Example 27-3: Shorthand formula - four or more specifically defined amino acids

A peptide of the formula (Gly-Gly-Gly-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 “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, if “X” is intended to represent “any amino acid”, then it should 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, 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
Example 28-1: Encoding nucleotide sequence and encoded amino acid sequence

A patent application describes the following sequences:

**Protein A**

```
caattcaggg tggtaaat atg gcg ccc aat acg caa acc gcc tct ccc cgc
Met Ala Pro Asn Thr Gln Thr Ala Ser Pro Arg
```

gcg ttg gcc gat tca tta atg cag ctg gca cga cag gtt tcc cga ctg
Ala Leu Ala Asp Ser Leu Met Gln Leu Ala Arg Gln Val Ser Arg Leu

```
gaa agc ggg cag tga atg acc atg att acg gat tca ctg gcc gtc gtt
Glu Ser Gly Gln Met Thr Met Ile Thr Asp Ser Leu Ala Val Val
```

tta caa cgt cgt gac tgg gaa aac cct ggc gtt acc cca ctt aat cgc
Leu Gln Arg Arg Asp Trp Glu Asn Pro Gly Val Thr Gln Leu Asn Arg

**Protein B**

```
ctt gca gca cat tgg tgt caa aaa taa taataacggg atgtactatt
Leu Ala Ala His Trp Cys Gln Lys
```

tatccctg atg ctg cgt cgt cag gtt aat gaa gtc gct taa gcaatcaatg
Met Leu Arg Arg Gln Val Asn Glu Val Ala

**Protein C**

```
tcgatgccg cgccagccgtt atcgaccaaa catatcataa
```

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 acids 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:

caattcagggtgtgaatatcgcccaaatcgcaaccccgctctcccccggcgttggtgaatcttgactacgttttacaacgtcgtggactgggaaaaccctggcgttacccaacttaatcgccttgcagcacattggtgtcaaaaataataataaccggatgtactaattatccctgatgctgcgtcgtcaggtgaatgaagtcgcttaagcaatcaatgtcggatgcggcgcgacgcttatccgaccaacatatcataa (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 5). 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 5 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, 87-90
Paragraph 29 – Representation of an “other” amino acid

Example 29-1: Most restrictive ambiguity symbol for an “other” amino acid

A patent application describes the following sequence:

Ala-Hse-X₁-X₂-X₃-X₄-Tyr-Leu-Gly-Ser

Wherein, X₁ = Ala or Gly,
X₂ = Ala or Gly,
X₃ = Ala or Gly,
X₄ = 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 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?

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”.

X₁-X₄ are variant positions, 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:

AXXXXXXYLGS (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.

Since amino acid Hse is not found in Annex I, Section 4, Table 4, a feature key “SITE” and a qualifier “NOTE” must be provided with the complete, unabbreviated name of homoserine as per ST.26 paragraph 30.

According to paragraph 27, because X₁-X₄ represent an alternative of only 2 amino acids, then further description is required. Paragraph 94 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 94-95
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, 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 17 specifically defined amino acids. There are 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?

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 must be included in a sequence listing as:

LEYCLKRWNETISHCAW (SEQ ID NO: 51)

A further description of the modified amino acid is required. 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 in position 9. The qualifier “NOTE” describes 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.

In addition, there is a disulfide bond between the two Cys residues. Therefore the feature key “DISULFID” is used to describe an intrachain crosslink. The location descriptors in the feature location element are the residue position numbers of the linked Cys residues in conjunction with the “join” location operator, “join(4,15)”. The qualifier NOTE is not mandatory.

Relevant ST.26 paragraph(s): 3(a), 7(b), 26, 29, 30, and Annex I, section 7, feature key 7.4
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: 52).

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-z₂-Lys-zₐ-Lys-z₃-Lys-zₐ-Lys-z₂-Lys

Where z is any amino acid, m=20, n=19-20, z₂ means that the pairs of Lysines are separated by any two amino acids, and z₃ means the pairs of 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; “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, 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):

KXXKXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXKXXK (SEQ ID NO: 53)

Wherein zₐ is equal to 20 “X’s”, with a further description that the “X” variable corresponding to position 30 can be deleted.

Alternatively, or in addition to the above, the sequence may be represented as:

KXXKXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXKXXK (SEQ ID NO: 54)

Wherein zₐ is equal to 19 “X’s”, with a further description that an “X” variable between position numbers 29 and 30 can be inserted.

According to paragraph 27, “X” will be construed as any one of “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, if “X” is intended to represent “any amino acid”, then it should 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 \( 20-22 \), \( n = 15-25 \), preferably \( 19-20 \), \( z_2 \) means that the pairs of Lysines are separated by any two amino acids, and \( z_3 \) means the pairs of 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 this amino acid is “X.” After considering the presence of “X” variables, the peptide contains 6 lysine residues that are enumerated and specifically defined, which is required 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:

\[ KXXKXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXKKKKK \] (SEQ ID NO: 55)

(where \( m = 25 \) and \( n = 25 \)), with a further description that up to 10 “X” residues in each of the “zm” or “zn” 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:

\[ KXXKXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXKKKKK \] (SEQ ID NO: 56)

(where \( m = 15 \) and \( n = 15 \)), with a further description that up to 10 “X” residues in each of the “zm” or “zn” 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 “A”, “R”, “N”, “D”, “C”, “Q”, “E”, “G”, “H”, “I”, “L”, “K”, “M”, “F”, “P”, “Q”, “S”, “U”, “T”, “W”, “Y”, or “V”, except where it is used with a further description in the feature table. Therefore, if “X” is intended to represent “any amino acid”, then it should 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 “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

Gly-Gly----Gly-Gly-Xaa-Xaa

where the symbol ---- is an undefined gap within the sequence, where Xaa is any amino acid, and the 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.

ST.26 paragraph 8 does not permit inclusion of either region adjacent to the undefined gap, since each region contains only two specifically defined amino acids.

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

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 Glycine 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 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

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: 57)

Preferably, 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 an N-terminal Gly-Gly and a gap of undefined length.”.

According to paragraph 27, “X” will be construed as any one of “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, if “X” is intended to represent “any amino acid”, then it should 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, 26, 27, and 37
Paragraph 55 – A nucleotide sequence that contains both DNA and RNA segments

Example 55-1: Combined DNA/RNA Molecule

A patent application describes the following oligonucleotide sequence:

AGACCTTcggagucuccuguaacagauagucaaaguagauC

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:

agaccttcggagtctcctgttgaaacagatagtcaaatagatc (SEQ ID NO: 92)

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 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,” which includes 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 87 – “CDS” Feature key**

**Example 87-1: 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:

```
atgaccggaaataaaacctgaaacctgattacgaaatattatatga (SEQ ID NO: 58)
```

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 “MTGNKPETDYEIL”. The application does not disclose the genetic code table that applies to the translation (see Annex 1, Section 9, Table 5). 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 5 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:

```
MTGNKPETDYEIL (SEQ ID NO: 59)
```

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, 87, 88, and 90
Example 87-2: 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 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 tgt tta tgt tgg ggg cct caa gtc caa ggc ttt atc ttt 144
Ser Arg Cys Trp Leu Trp Cys Gly Pro Gln Val 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 Gly Lys Glu Gly Gly Gly Asp Arg Arg Ala Glu Ala Ser Pro
50 55 60

cag gag ttt tgt gaa tgc act tgt 216
Gln Glu Phe Trp Glu Cys Thr Trp
65 70
```

Figure 1 - partial coding sequence of the Homo sapiens 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 10 specifically defined nucleotides and must be included in a sequence listing.

The amino acid sequence contains more than 4 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:

catcacgcagcagaatgtggattttgtcctcaacaatggcaagttctacgtgggagtctgtgcatttgtgagggtccagctgaaggatggttcatatcaagatgttggtatatggtgatggtgctcaagctcaaggtcttatctttggagaaggcaaggaaggaggcggtgacagacgggctgaagcgagccctcaggagttttgggaatgcacttg  (SEQ ID NO: 93)

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 “&lt;” and “&gt;”, 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 5). 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 5 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:

HHAAECGFCPQWQLRGLSCIEGPAEGWFIISRCLWCPQVQFIFGEKGGGDARRAEASPQEFWECTW  (SEQ ID NO: 94)

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, 87, and 90
Paragraph 90 – Amino acid sequence encoded by a coding sequence

Example 90-1: 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 TCC GCA GCC TTG CTT TCC GCT GTC ACT CTC GCG ETC TCG
Met Lys Thr Ala Ala Leu Leu Ser Ala Val Thr Leu Ala Leu Ser

GTG CCC GCC CAG GCC GCT GTC TGG AGT CAA T GTAAGTGCG C TGCTTTTCA
Val Arg Ala Gln Ala Ala Val Trp Ser Gln

TTGATA CGAG ACTCTACGCC GAGCTGACGT GCTACC GTAT AG GT GCC GGT ACA
Cys Gly Gly Thr

CCG GGT TGG ACG GCC GAG ACC ACT TGC GTT GCT GGT TCG TGT ACC
Pro Gly Trp Thr Gly Glu Thr Thr Cys Val Ala Gly Ser Val Cys Thr

tcc ttc aag tca GGT GCG ACT TTAAT CC GTG ATC GCG CCG CCA GCA
Leu Ser Ser Ser

tgacgat gg cc ttc aat g tca tac tct cca tgc ctt ccc gcc tcc gca acg
Ser Tyr Ser Gln Cys Val Pro Gly Ser Ala Thr

tcc aag gct ccc gcc gcc ctc tca ggc aca act tca gcc ccc gca cct
Ser Ser Ala Pro Ala Ala Pro Ser Ala Thr Thr Ser Gly Pro Ala Pro

gac gac gga acg tgc tcc gcc acc ggc tgg ccc cca ttg acc tga
Thr Asp Gly Thr Cys Ser Ala Ser Gly Ala Trp Pro Pro Leu Thr Thr
```

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 10 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
cctctacgccgacgtgctaccgtataggtggcggtacaccgggttggacgggcgagaccacttgcgttgctggttcggtttgtacctccttgagctcagtgag
cgactttcaatccgtcgtcattgctcctcatgtattgacgattggccttcatagtcatactctcaatgcgttccgggctccgcaacgtccagcgctccggcggccccctc
agcgacaacttcagccccgcacccacaggaacgtgctcgccagccggccatggccagtgggccgccagtga (SEQ ID NO: 74)
```

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”. 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 5). 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 5 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
```

Relevant ST.26 paragraphs: 7, 26, 28, 57, and 87-90
Paragraph 91 – Primary sequence and a variant, each enumerated by its residues

Example 91-1: Representation of enumerated variants

The description includes the following sequence alignment.

\[\begin{align*}
D. \text{ melanogaster} &: \text{ACATTGAATCTCATACTTT} \\
D. \text{ virilis} &: \ldots-\ldots G\ldots C\ldots -\ldots G\ldots \ldots \\
D. \text{ simulans} &: \text{GT}\ldots G\ldots C\ldots GT\ldots SG\ldots T\ldots G\ldots \\
\end{align*}\]

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 \textit{D. virilis} and \textit{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 \textit{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 \textit{D. melanogaster} and \textit{D. simulans} contain twenty-two enumerated and specifically defined nucleotides, whereas the nucleotide sequence of \textit{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?

\textit{Drosophila melanogaster} sequence must be included in a sequence listing as:
\text{acattgaatctcatacttt} (SEQ ID NO: 60)

\textit{Drosophila virilis} sequence must be included in a sequence listing as:
\text{acatggatcccacgacttt} (SEQ ID NO: 61)

\textit{Drosophila simulans} sequence must be included in a sequence listing as:
\text{gtatggcgtcgtatsgtagttt} (SEQ ID NO: 62)

Relevant ST.26 paragraphs: 7(a), 13, and 91
Example 91-2: Representation of enumerated variants

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”.

<table>
<thead>
<tr>
<th>Position</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sequence</td>
<td>A</td>
<td>V</td>
<td>L</td>
<td>T</td>
<td>Y</td>
<td>L</td>
<td>R</td>
<td>G</td>
<td>E</td>
</tr>
<tr>
<td>Variant 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>A</td>
</tr>
<tr>
<td>Variant 2</td>
<td>P</td>
<td>P</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Variant 3</td>
<td>A</td>
<td>I</td>
<td>G</td>
<td>Y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Variant 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-</td>
</tr>
</tbody>
</table>

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: 76)
AVLTYLRGA (SEQ ID NO: 77)
AVPTYPRGE (SEQ ID NO: 78)
AVAIGYRGE (SEQ ID NO: 79)
AVLTYLGE (SEQ ID NO: 80)

Relevant ST.26 paragraphs: 7(b), 26, and 91
Example 91-3: Representation of a consensus sequence

A patent application includes Figure 1 with the following multiple sequence alignment.

Consensus:  LEGnEQFINAakIIRHkYnrkDlnNDImlIK

The consensus sequence includes upper case letters to represent conserved amino acid residues, while the 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 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 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 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 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:

LEGXEQFINAXXAIIRHkYXIXTBNNDImlIK (SEQ ID NO: 81)

According to paragraph 27, the symbol “X” will be construed as any one of “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:

LEGNEQFINAAkIIRHkYDRktLNNNDImlIK (SEQ ID NO: 82)
LEGTEQFINAAkIIRHkYDRktVNNNDImlIK (SEQ ID NO: 83)
LEGTEQFINAAkIIRHkYNRnTLDNDImlIK (SEQ ID NO: 84)
LEGTEQFINATkIIRHkYNRnTLDNDImlIK (SEQ ID NO: 85)
LEGTEQFINATkIIRHkYNRnTLDNDImlIK (SEQ ID NO: 86)
LEGTEQFINATkIIRHkYNRnTLDNDImlIK (SEQ ID NO: 87)
LEGTEQFINATkIIRHkYNRnTLDNDImlIK (SEQ ID NO: 88)

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, 91, and 95
Paragraph 92 – Variant sequence disclosed as a single sequence with enumerated alternative residues

Example 92-1: 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 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: 63)

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: 64)

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, 92, and 95
Paragraph 93(a) – A variant sequence disclosed only by reference to a primary sequence with multiple independent variations

Example 93(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: 65)

According to paragraph 27, “X” will be construed as any one of “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, if “X” is intended to represent “any amino acid”, then it should 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: 66) 
GLPTRIC (SEQ ID NO: 67) 
GLPDRIC (SEQ ID NO: 68)

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 93(a)
Paragraph 93(b) – A variant sequence disclosed only by reference to a primary sequence with multiple interdependent variations

Example 93(b)-1: Representation of individual variant sequences with multiple interdependent variations

A patent application describes the following consensus sequence:

\[ \text{cgaat} \text{gn1} \text{cccactacgaatgn2} \text{caca} \text{gaatgn3} \text{cccaca} \]

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 \( n_2 \) and \( n_3 \) are \( t, g, \) or \( c \);
- if \( n_1 \) is \( t \), then \( n_2 \) and \( n_3 \) are \( a, g, \) or \( c \);
- if \( n_1 \) is \( g \), then \( n_2 \) and \( n_3 \) are \( t, a, \) or \( c \);
- if \( n_1 \) is \( c \), then \( n_2 \) and \( n_3 \) 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:

\[ \text{cgaatgnccca} \text{ctacgaatgn} \text{caca} \text{gaatgn} \text{cccaca} \] (SEQ ID NO: 69)

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 to this document. Therefore, according to ST.26 paragraph 93(b), the additional embodiments should be included in a sequence listing as four separate sequences, each with its own sequence identification number:

\[ \text{cgaatgccccac} \text{tacgaatgncaca} \text{tgncccaca} \] (SEQ ID NO: 70)
\[ \text{cgaatgtccca} \text{ctacgaatgvca} \text{gaatgvcccaca} \] (SEQ ID NO: 71)
\[ \text{cgaatgccccac} \text{tacgaatgchcaca} \text{tghcccaca} \] (SEQ ID NO: 72)
\[ \text{cgaatgccccac} \text{tacgaatgdcaca} \text{tgdcccaca} \] (SEQ ID NO: 73)

(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, \( n_2 \) and \( n_3 \) must not be represented by "n" in the sequence.

**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 93(b)

[Appendix of Annex VI follows]
APPENDIX

GUIDANCE DOCUMENT SEQUENCES IN XML

The Appendix is available at:

[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 1.3

Adopted by the Committee on WIPO Standards (CWS)
at its seventh session on July 5, 2019

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 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.

Scenario 4

ST.26 has the mandatory feature keys – “source” for all nucleotide sequences and “SOURCE” for all amino acid sequences, each with two mandatory qualifiers. 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 qualifiers 6.44 organism and 6.38 mol_type (see ST.26 paragraph 75)

<table>
<thead>
<tr>
<th>Qualifier</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>mol_type</td>
<td>genomic DNA</td>
</tr>
<tr>
<td></td>
<td>genomic RNA</td>
</tr>
<tr>
<td></td>
<td>mRNA</td>
</tr>
<tr>
<td></td>
<td>tRNA</td>
</tr>
<tr>
<td></td>
<td>rRNA</td>
</tr>
<tr>
<td></td>
<td>other DNA (applies to synthetic molecules)</td>
</tr>
<tr>
<td></td>
<td>other RNA (applies to synthetic molecules)</td>
</tr>
<tr>
<td></td>
<td>transcribed RNA</td>
</tr>
<tr>
<td></td>
<td>viral cRNA</td>
</tr>
<tr>
<td></td>
<td>unassigned DNA (applies where in vivo molecule is unknown)</td>
</tr>
<tr>
<td></td>
<td>unassigned RNA (applies where in vivo molecule is unknown)</td>
</tr>
</tbody>
</table>

### Amino acid sequences

ST.26 – feature key 7.30 SOURCE; mandatory qualifiers 8.3 ORGANISM and 8.1 MOL_TYPE (see ST.26 paragraph 75)

<table>
<thead>
<tr>
<th>Qualifier</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MOL_TYPE</td>
<td>protein</td>
</tr>
</tbody>
</table>

**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” or “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.
<table>
<thead>
<tr>
<th>No.</th>
<th>ST.25 Feature key &lt;221&gt;</th>
<th>ST.26 equivalent</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Feature key</td>
<td>Qualifier</td>
</tr>
<tr>
<td>1</td>
<td>allele</td>
<td>allele</td>
</tr>
<tr>
<td>2</td>
<td>attenuator</td>
<td>regulatory</td>
</tr>
<tr>
<td></td>
<td></td>
<td>regulatory_class</td>
</tr>
<tr>
<td>3</td>
<td>CAAT_signal</td>
<td>regulatory</td>
</tr>
<tr>
<td></td>
<td></td>
<td>regulatory_class</td>
</tr>
<tr>
<td>4</td>
<td>conflict</td>
<td>misc_feature</td>
</tr>
<tr>
<td>5</td>
<td>enhancer</td>
<td>regulatory</td>
</tr>
<tr>
<td></td>
<td></td>
<td>regulatory_class</td>
</tr>
<tr>
<td>6</td>
<td>GC_signal</td>
<td>regulatory</td>
</tr>
<tr>
<td></td>
<td></td>
<td>regulatory_class</td>
</tr>
<tr>
<td>7</td>
<td>LTR</td>
<td>mobile_element</td>
</tr>
<tr>
<td></td>
<td></td>
<td>rpt_type</td>
</tr>
<tr>
<td>8</td>
<td>misc_signal</td>
<td>regulatory</td>
</tr>
<tr>
<td></td>
<td></td>
<td>regulatory_class</td>
</tr>
<tr>
<td>9</td>
<td>mutation</td>
<td>variation</td>
</tr>
<tr>
<td>10</td>
<td>old_sequence</td>
<td>misc_feature</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>polyA_signal</td>
<td>regulatory</td>
</tr>
<tr>
<td></td>
<td></td>
<td>regulatory_class</td>
</tr>
<tr>
<td>12</td>
<td>promoter</td>
<td>regulatory</td>
</tr>
<tr>
<td></td>
<td></td>
<td>regulatory_class</td>
</tr>
<tr>
<td>13</td>
<td>RBS</td>
<td>regulatory</td>
</tr>
<tr>
<td></td>
<td></td>
<td>regulatory_class</td>
</tr>
<tr>
<td>14</td>
<td>repeat_unit (a)</td>
<td>misc_feature</td>
</tr>
<tr>
<td></td>
<td>when repeat_region not used</td>
<td></td>
</tr>
<tr>
<td></td>
<td>repeat_region</td>
<td>rpt_unit_range</td>
</tr>
<tr>
<td></td>
<td></td>
<td>note</td>
</tr>
<tr>
<td>15</td>
<td>satellite</td>
<td>repeat_region</td>
</tr>
<tr>
<td></td>
<td></td>
<td>satellite</td>
</tr>
<tr>
<td>16</td>
<td>scRNA</td>
<td>ncRNA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ncRNA_class</td>
</tr>
<tr>
<td>17</td>
<td>snRNA</td>
<td>ncRNA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ncRNA_class</td>
</tr>
<tr>
<td>18</td>
<td>TATA_signal</td>
<td>regulatory</td>
</tr>
<tr>
<td></td>
<td></td>
<td>regulatory_class</td>
</tr>
<tr>
<td>19</td>
<td>terminator</td>
<td>regulatory</td>
</tr>
<tr>
<td></td>
<td></td>
<td>regulatory_class</td>
</tr>
<tr>
<td>20</td>
<td>3'clip</td>
<td>misc_feature</td>
</tr>
<tr>
<td>21</td>
<td>5'clip</td>
<td>misc_feature</td>
</tr>
<tr>
<td>22</td>
<td>-10_signal</td>
<td>regulatory</td>
</tr>
<tr>
<td></td>
<td></td>
<td>regulatory_class</td>
</tr>
<tr>
<td>23</td>
<td>-35_signal</td>
<td>regulatory</td>
</tr>
<tr>
<td></td>
<td></td>
<td>regulatory_class</td>
</tr>
</tbody>
</table>

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. In such a case, the narrower ST.25 feature will be afforded priority to the earlier application. However, the full breadth of the broader ST.26 feature key/qualifier, e.g., regulatory/regulatory_class, will not be afforded priority to the earlier application.
<table>
<thead>
<tr>
<th>No.</th>
<th>Feature key &lt;221&gt;</th>
<th>ST.25 Feature key</th>
<th>ST.26 equivalent</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>NON_CONS</td>
<td>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.</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>SIMILAR</td>
<td>REGION</td>
<td>“SIMILAR” and &lt;223&gt; value if present</td>
</tr>
<tr>
<td>26</td>
<td>THIOETH</td>
<td>CROSSLINK</td>
<td>“THIOETH” and &lt;223&gt; value if present</td>
</tr>
<tr>
<td>27</td>
<td>THIOLEST</td>
<td>CROSSLINK</td>
<td>“THIOLEST” and &lt;223&gt; value if present</td>
</tr>
<tr>
<td>28</td>
<td>VARSPLIC</td>
<td></td>
<td>Discussed in a Scenario 13 below</td>
</tr>
<tr>
<td>29</td>
<td>ACETYLATION</td>
<td>MOD_RES</td>
<td>“ACETYLATION” and &lt;223&gt; value if present</td>
</tr>
<tr>
<td>30</td>
<td>AMIDATION</td>
<td>MOD_RES</td>
<td>“AMIDATION” and &lt;223&gt; value if present</td>
</tr>
<tr>
<td>31</td>
<td>BLOCKED</td>
<td>MOD_RES</td>
<td>“BLOCKED” and &lt;223&gt; value if present</td>
</tr>
<tr>
<td>32</td>
<td>FORMYLATION</td>
<td>MOD_RES</td>
<td>“FORMYLATION” and &lt;223&gt; value if present</td>
</tr>
<tr>
<td>33</td>
<td>GAMMA-CARBOXYGLUTAMIC ACID HYDROXYLATION</td>
<td>MOD_RES</td>
<td>“GAMMA-CARBOXYGLUTAMIC ACID HYDROXYLATION” and &lt;223&gt; value if present</td>
</tr>
<tr>
<td>34</td>
<td>METHYLATION</td>
<td>MOD_RES</td>
<td>“METHYLATION” and &lt;223&gt; value if present</td>
</tr>
<tr>
<td>35</td>
<td>PHOSPHORYLATION</td>
<td>MOD_RES</td>
<td>“PHOSPHORYLATION” and &lt;223&gt; value if present</td>
</tr>
<tr>
<td>36</td>
<td>PYRROLIDONE CARBOXYLIC ACID</td>
<td>MOD_RES</td>
<td>“PYRROLIDONE CARBOXYLIC ACID” and &lt;223&gt; value if present</td>
</tr>
</tbody>
</table>
### 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

<table>
<thead>
<tr>
<th>Feature Key</th>
<th>Mandatory Qualifier</th>
<th>Qualifier</th>
<th>Qualifier value</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.12 - misc_binding</td>
<td>6.3 - bound_moiety</td>
<td>NOTE</td>
<td>&quot;SULFATATION&quot; and &lt;223&gt; value if present</td>
</tr>
<tr>
<td>5.30 - protein_bind</td>
<td>6.3 - bound_moiety</td>
<td>NOTE</td>
<td>Information required by ST.26 Annex I MOD_RES Feature Key Comment, if possible (without added subject matter)</td>
</tr>
</tbody>
</table>

---

2 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

<table>
<thead>
<tr>
<th>Feature Key</th>
<th>Mandatory Qualifier</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.2 – BINDING</td>
<td>8.2 – NOTE</td>
</tr>
<tr>
<td>7.4 – CARBOHYD</td>
<td>8.2 – NOTE</td>
</tr>
<tr>
<td>7.10 – DISULFID</td>
<td>8.2 – NOTE</td>
</tr>
<tr>
<td>7.11 – DNA_BIND</td>
<td>8.2 – NOTE</td>
</tr>
<tr>
<td>7.12 – DOMAIN</td>
<td>8.2 – NOTE</td>
</tr>
<tr>
<td>7.16 – LIPID</td>
<td>8.2 – NOTE</td>
</tr>
<tr>
<td>7.17 – METAL</td>
<td>8.2 – NOTE</td>
</tr>
<tr>
<td>7.18 – MOD_RES</td>
<td>8.2 – NOTE</td>
</tr>
<tr>
<td>7.23 – NP_BIND</td>
<td>8.2 – NOTE</td>
</tr>
<tr>
<td>7.29 – SITE</td>
<td>8.2 – NOTE</td>
</tr>
<tr>
<td>7.39 – ZN_FING</td>
<td>8.2 – NOTE</td>
</tr>
</tbody>
</table>

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 “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.

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).

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:

```xml
<220>
<221> CDS
<222> (1)..(571)
</220>
<220>
<221> CDS
<222> (639)..(859)
</220>
```

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:

```xml
<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:

<table>
<thead>
<tr>
<th>Type</th>
<th>ST.25 Feature Key</th>
<th>Potential ST.26 Equivalent</th>
</tr>
</thead>
<tbody>
<tr>
<td>NA</td>
<td>“Custom” feature key</td>
<td>misc_feature</td>
</tr>
<tr>
<td>AA</td>
<td>“Custom” feature key</td>
<td>SITE or REGION</td>
</tr>
</tbody>
</table>
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” or “SOURCE” requires the qualifier “organism” or “ORGANISM”, whose value must be indicated as “synthetic construct”, rather than “Artificial Sequence”.

Recommendation:
The value for the ST.26 qualifier “organism” or “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” or “NOTE” (of the feature key “source” or “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” or “SOURCE” requires the qualifier “organism” or “ORGANISM”, whose value must be indicated as “unidentified”, rather than “Unknown”.

Recommendation:
The value for the ST.26 qualifier “organism” or “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” or “NOTE” (of the feature key “source” or “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]