



HARMONIZED SYSTEM
REVIEW SUB-COMMITTEE

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O. Eng.

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POSSIBLE AMENDMENTS TO THE STRUCTURED NOMENCLATURE
TO HEADING 29.41 AND THE EXPLANATORY NOTES TO CHAPTER 29
(PROPOSAL BY THE MEXICAN ADMINISTRATION)
(Item III.B.1 on Agenda)

Reference document :

NS0060E2, Annex A/12 (SSC/17 – Report)

I. BACKGROUND

1. By letter of 17 May 2002, the Mexican Customs Administration has presented a proposal to amend the structured nomenclature to heading 29.41 and the Explanatory Notes to Chapter 29.

II. NOTE FROM THE MEXICAN ADMINISTRATION

“Background :

2. The term “derivatives” appears in the Nomenclature in headings 29.03 through 29.11 and 29.13 through 29.20 in a limitative context with regard to “halogenated, sulphonated, nitrated or nitrosated derivatives”, which are understandable in view of the fact that no other chemical derivatives (i.e., hydroxylated, aminated, etc.) are allowed in these headings. Definition of those “derivatives” are found in paragraph (F) of the General Explanatory Note to Chapter 29 (on page 373) : “**The halogenated, sulphonated, nitrated and nitrosated derivatives are formed by substitution of one or more hydrogen atoms in the parent compound ...**”.

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3. The Explanatory Note to Sub-Chapter IX, nitrogen-function compounds, contains limitative definitions of the term “derivatives” such as the Subheading Explanatory Note for subheadings 2921.42 to 2921.49 which reads : **“Hydrocarbon derivatives of an aromatic monoamine are derivatives obtained by the substitution of one or both hydrogens of the amine nitrogen only by an alkyl or cycloalkyl group...”** (page 431).
4. Heading 29.28 is dedicated to “Organic derivatives of hydrazine or of hydroxylamine” and, again, those are formed by replacement of one or more hydrogen atoms of the parent compound (Explanatory Notes, page 442).
5. Derivatives of subheadings 2933.11, 2933.21 and 2933.52 are ruled by a Subheading Explanatory Note (page 458) which comprises the chemical definition of a “derivative”, i.e., **should have the functional groups of the parent compound unmodified; should retain the number and position of double bonds; retain the substituents and have further substitutions of hydrogen atoms only.**
6. On the other hand, derivatives of compounds included in Sub-Chapters XI and XII are ruled by a General Explanatory Note (page 461 and 483, respectively) in which **“the term “derivatives” refers to chemical compounds which could be obtained from a starting compound from the heading concerned and which retain the essential characteristics of the parent compound, including its basic chemical structure”**. This definition, if not as precise as the one included in the previous paragraph, gives a broad and rough idea of the type of compounds that could fall under the term “derivatives”.
7. However, heading 29.37 includes the “structural analogues of hormones, prostaglandins... etc”. The term “analogue” is defined on page 470 of the Explanatory Notes as **“Those chemicals having a close structural relationship to the parent compound, but which are not considered to be derivatives“**.

Proposal :

8. Considering that :
 - (i) The term “derivative” is reasonably well defined in the various headings of Chapter 29 outlined above;
 - (ii) The term “structural analogue” as defined on page 470 of the Explanatory Notes is different from “derivatives” in its context and definition;
 - (iii) Sub-Chapter XIII does not contain any reference to the term “derivatives”, except in the case of heading 29.40 in which the legal terms of the heading allow the ethers, acetals, esters and its salts, functionalities that are well defined in the general part of the Explanatory Notes to Chapter 29; and
 - (iv) Heading 29.41 contains 5 subheadings whose terms include the “derivatives” of penicillins, streptomycins, tetracyclines, chloramphenicol and erythromycin and that only in the case of penicillins derivatives are defined by the respective Subheading Explanatory Note (page 491);

it is necessary to include a definition of the term “derivative” to be applied to Sub-Chapter XIII and, since it seems that the general opinion of the Scientific Sub-Committee is to include structural analogues of chloramphenicol (i.e., thiamphenicol and florfenicol) in subheading 2941.40 (see Annex A/12 to Doc. NS0060E2 – SSC/17 - Report), it could be convenient to

insert the proper definition of the term “structural analogue” and to amend the terms of subheadings 2941.10 through 2941.50 as well.

Insert on page 489 of the Explanatory Notes after the title Other Organic Compounds the following :

9. “In this Sub-Chapter, the term “derivatives” refers to chemical compounds which could be obtained from a starting compound of the heading concerned and which retain the essential characteristics of the parent compound, including its basic chemical structure.
10. On the other hand, the term “structural analogue” refers to chemical compounds having a close structural relationship to the parent compound but which are not considered as derivatives. Differences between parent compounds and analogues could be on replacement of certain functional groups, hydrogenation or dehydrogenation and replacing some atoms in the ring by others (heteroatoms).”

Delete and insert on page 490 of the Explanatory Notes :

"29.41 – ANTIBIOTICS (+).

2941.10 – Penicillins and their derivatives with a penicillanic acid structure; salts thereof

2941.20 – Streptomycins and their derivatives; salts thereof

2941.30 – Tetracyclines, their derivatives and structural analogues; salts thereof

2941.40 – Chloramphenicol, their derivatives and structural analogues; salts thereof

2941.50 – Erythromycin and its derivatives; salts thereof

2941.90 – Other”.

III. SECRETARIAT COMMENTS

11. The Mexican Administration is proposing to amend the text of subheadings 2941.30 and 2941.40 to include structural analogues of tetracyclines and salts thereof and structural analogues of chloramphenicol and salts thereof in these new subheadings, for the reasons mentioned in paragraph 8 above. It should be noted that these structural analogues are presently classified in subheading 2941.90.
12. The Secretariat agrees with the Mexican Administration that the proposed amendment of the structured nomenclature to heading 29.41 would require clarification of the new term “structural analogues” of tetracyclines and chloramphenicol. For this purpose, the approach to define the term “structural analogues” by means of a definition of the term “derivatives” could be acceptable, since the same approach has already been used in Sub-Chapter XI of Chapter 29 to describe structural analogues of hormones as compared with their derivatives. Nevertheless, both proposed definitions raised a number of questions.

13. Chapter 29 follows the order from the simplest and well defined products to more complicated products. According to Note 1 (c) to Chapter 29, products of Sub-Chapters XI, XII or the sugar ethers, sugar acetals, sugar esters, their salts and products of headings 29.40 and 29.41 do not have to be chemically defined. Consequently, Sub-Chapter XIII being the last Sub-Chapter of Chapter 29 generally comprises products of great complexity and diversity.
14. The **Mexican** Administration proposes to define the term “derivatives” in the General Explanatory Note to Sub-Chapter XIII using the same wording that already appears in Sub-Chapters XI and XII of Chapter 29. This means that one general definition of the term “derivatives” would be applied to headings 29.40, 29.41 and 29.42, as follows :
- “In this Sub-Chapter, the term “derivatives” refers to chemical compounds which could be obtained from a starting compound of the heading concerned and which retain **the essential characteristics** of the parent compound, including its **basic chemical structure** (emphasis added).”
15. With respect to the actual wording suggested, questions would arise as to what are “the **essential characteristics** of the parent compound” to be retained by derivatives and what is “**the basic chemical structure**” of the parent compound. Since Sub-Chapter XIII includes products of great structural diversity, such as antibiotics, sugars and other organic compounds of residual heading 29.42, these elements of the proposed definition could be interpreted in a rather subjective manner. The Secretariat feels that in order to ensure uniform application, these elements should be clarified for each group of structurally related compounds of Sub-Chapter XIII, preferably in the relevant parts of the Explanatory Notes to individual headings.
16. In this connection, the Secretariat would like to recall that the term “derivatives” in Sub-Chapter XIII specifically appears only in the legal texts of the five subheadings 2941.10 to 2941.50 and a Subheading Explanatory Note already exists with regard to subheading 2941.10. This Subheading Explanatory Note clarifies the scope of subheading 2941.10, which also includes “derivatives” of penicillins with a penicillanic acid structure.
17. Furthermore, the expression “which **could** be obtained from a starting compound of the heading concerned” (emphasis added) in the proposed definition of “derivatives” allows the term “derivatives” to be interpreted quite flexibly, i.e., to be understood that “derivatives” could also be obtained from another source than from a starting compound of the heading concerned. If that would be the intention of the proposed definition, the same interpretation of “derivatives” should also apply with regard to the term “derivatives” in Sub-Chapters XI and XII, where the same wording already appears in the Explanatory Notes.
18. By analogy, using the word “could” in the description of differences between parent compounds and analogues, as proposed in the last sentence of the new General Explanatory Note to Sub-Chapter XIII by the **Mexican** Administration (see paragraph 10 above), would provide a very vague interpretation of that General Explanatory Note.

19. As regards the term “analogue”, the following descriptions have been taken from *The New Shorter Oxford English Dictionary*, *Webster’s New World Dictionary of the American Language* and *Mc Graw-Hill Dictionary of Scientific and Technical Terms*.

(The New Shorter Oxford English Dictionary – 1993 edition)

Analogue = [1 . . .]; 2 *Chem.* A compound with a molecular structure closely similar to that another

Analogy = [1 . . .]; 8 *Biol.* Resemblance of form or function without fundamental identity

(Webster’s New World Dictionary of the American Language - Second college edition, 1970)

Analogy = 1. Similarity in some respects between things otherwise unlike; partial resemblance [2 . . .]; 3. *Biol.* Similarity in function between parts dissimilar in origin and structure: cf. HOMOLOGY

(Mc Graw-Hill Dictionary of Scientific and Technical Terms - Fifth edition, 1994)

Analog = [CHEM.] A compound whose structure is similar to that of another compound but whose composition differs by one element.

20. From the descriptions given above it can be seen that in connection with biological systems, the term “analogy” is related to resemblance or similarity of form or function. According to the Explanatory Note to heading 29.41 (first paragraph on page 490), antibiotics are substances secreted by living micro-organisms which have the effect of killing other micro-organisms or inhibiting their growth and which are used principally for their powerful inhibitory effect on pathogenic micro-organisms. Hence, the connection of antibiotics to biological systems being obvious, their biological activity should not be omitted when considering the similarity between antibiotics and their structural analogues.
21. In general, the biological activity of antibiotics is closely connected to the exact structural arrangement of a molecule or a part of a molecule. Even a minor structural change of a parent compound could lead to changes in potency or in spectrum of biological activity of a resultant structural analogue or a derivative. Thus, a structural analogue/derivative can still have some anti-microbial activity but acts specifically against other types of micro-organisms than the parent compound. Consequently, it may also have different therapeutic uses. In some cases, its biological activity can be lost depending on the type of the structural change effected.
22. The Secretariat therefore feels that the question as to whether the biological activity of a structural analogue/derivative of a particular antibiotic should be the same as, or similar to a certain extent, to that of a parent compound, should be studied by the Sub-Committee.
23. The Sub-Committee should also study whether to provide one general definition of “derivatives” and “structural analogues” in the General Explanatory Note to Sub-Chapter XIII, as proposed by Mexico, or to clarify these terms separately for individual headings of Sub-Chapter XIII, where necessary. In the latter case, the possible creation of separate definitions of individual groups of compounds in the Explanatory Note to heading 29.41 could also be considered. In this context, the Sub-Committee should express its preference as to whether to amend the Explanatory Notes to individual headings or to create the relevant Subheading Explanatory Notes.

24. In paragraph 8 above the Mexican Administration refers to the possible amendment of the terms of subheadings 2941.10 through 2941.50. However, the proposal as set out in paragraph 10 above, only includes amendments to subheadings 2941.30 and 2941.40. The Sub-Committee should therefore consider whether the insertion of the term “structural analogues” would be required for all of the subheadings 2941.10 to 2941.50.
25. In conclusion, the Secretariat would leave it to the Sub-Committee to decide whether :
- (i) the insertion of the term “structural analogues”, as proposed by Mexico, would be desirable for subheadings 2941.10 to 2941.50;
 - (ii) to provide one general definition of “derivatives” and “structural analogues” in the General Explanatory Note to Sub-Chapter XIII, as proposed by Mexico, or to clarify these terms separately for individual headings and how to define these terms;
 - (iii) to amend the Explanatory Notes to individual headings or to create relevant Subheading Explanatory Notes;
 - (iv) further action should be taken with regard to a possible study of biological activity of structural analogues/derivatives of particular antibiotics.
26. In the view of technical nature of this matter, the Sub-Committee may wish to submit the question first to the Scientific Sub-Committee for consideration.

IV. CONCLUSION

27. The Review Sub-Committee is invited to consider the proposed amendments to the structured nomenclature to heading 29.41 and the Explanatory Notes to Chapter 29, taking into account the Note from Mexican Administration and the Secretariat's comments above.
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