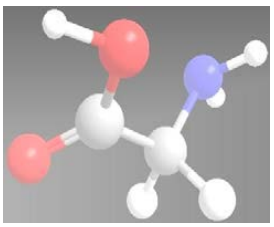
USAN INSIDER



Volume 9, Issue 3

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USAN Website Links:

USAN Requirements for Monoclonal Antibodies

The USAN Program has recently changed the materials to be submitted for monoclonal antibodies. After you receive your USAN file number, please send a copy of this information electronically to gail.karet@ama-assn.org. The following items are now required:

- ✓ Complete mature amino acid sequence in a Microsoft Word document
- ✓ Please ensure that the CAS Registry information includes the sequence for disulfide bridges and glycosylations
- ✓ Single-letter codes for each amino acid, displayed in groups of 10 characters with 5 groups per line and a number indicating the position of the last amino acid at the end of each line
- ✓ Glycosylation patterns, including site and type of sugar, etc.
- ✓ Precursor nucleotide sequence with spaces between codons and translation, with numbered lines
- ✓ CDR-IMGT and sequence analysis of the variable regions showing percentage of human content (if –ximab, -zumab, or -umab is requested; >90% -umab, -zumab is typically >85%, <85% -ximab)
- ✓ CDR-Kabat (sequence and residue range)
- ✓ IG class and subclass, IG format
- ✓ Species or taxonomy related structure (chimeric, humanized, etc.)
- ✓ Name and/or structure of targeted antigen
- ✓ List of all disulfide bridges and their locations
- ✓ Expression system
- ✓ Clone name(s) and laboratory code name(s)
- ✓ If appropriate, the closest human V, J, and C genes and alleles (results obtained with IMGT/DomainGapAlign tool)
    - o For the V-domains, if the domains are nominally human (e.g. produced from human antibodies, EBV immortalization of human B-cells, human phage display libraries, transgenic mice with human V-domain genes, or similar), the closest human gene/allele should be given

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- If the V-domains have been humanized by CDR-grafting onto a human framework, the closest human gene/allele to the parent human framework should be given
- Otherwise the closest germline (human or other species) should be given

✓ If the If the terminal lysine is absent in the heavy chain amino acid sequence, a statement of the fabricant confirming that indeed there is no lysine codon in the nucleotide sequence (if not the lysine should be added in the amino acid sequence mentioning the posttranslational modification clipping)

✓ If relevant, amino acid differences with the native sequence (for a monoclonal antibody: constant region amino acid changes by comparison with the closer genomic C gene and allele)

USAN Application Wire Transfers

We have recently received notification from our accounting department that some manufacturers are sending their USAN application fees to the wrong banking institution. Please use the following information in the hyperlink below when making a wire transfer to the USAN Program or contact mary.haynes@ama-assn.org for instructions.

✓ **USAN Program Wire Transfer and ACH Directions**

Conjugated Monoclonal Antibody Naming Policy starting January 1, 2019 (New Policy)

✓ **USAN Application Flowchart**

Effective January 1, firms can only request a USAN modified for salts or esters of substance that have already received a USAN (or for which a USAN application has been submitted) and that do not have a peptide or nucleotide sequence. Substances that are not salts or esters but are related require additional work for chemical review and/or Council balloting. Consequently, related compounds that are not salts or esters are treated as single entities. Examples include stereoisomers or enantiomers isolated from a racemic mixture, antibody-drug conjugates, oligonucleotides or other substances where the chemical structure or sequence have changed and another name is required.

The USAN Program is often asked which form to fill out in specific situations.

- For a small molecule and its salt or ester, please use form A.
- For all substances for which there is a DNA, RNA or amino acid sequence, please use form F. When more than one name is requested, a separate form F should be filled out for each substance. Therefore, for example, an antisense oligonucleotide and its salt, or an antibody and an antibody-drug conjugate would require two applications using form F.
- Firms needing to revise the chemical, company, indication or other information associated with a substance should use form D.
- For a second name for the salt or ester of a substance that already has a USAN (or for which a USAN has been requested), form C should be used.
- For contact lens polymers, form E should be used.
- For all other substances, please use form B.

Turn Back the Clock – AMA/FDA Nomenclature Collaboration

Over the last century, a close and collaborative relationship has developed between the American Medical Association (AMA) and the U.S. Food and Drug Administration (FDA). The AMA was one of the first organizations to recognize deficiencies in the 1906 Pure Food and Drugs Act and advocate for necessary changes in food and drug legislation. According to the FDA, the "basis of this law rested on the regulation of product labeling rather than premarket approval. Drugs, defined in accordance with the standards of strength, quality, and purity in the United States Pharmacopeia and the National Formulary, could not be sold in any other condition unless the specific variations from the applicable standards were plainly stated on the label".

In the regulation of drugs, misbranding became a source of considerable controversy. The FDA was put into the position of having to prove that a drug manufacturer intended to defraud customers. This resulted in many lost court cases although "seizures of misbranded and adulterated drugs" increased throughout the 20s and 30s".

The AMA recognized that change was needed. In 1933, before the Food, Drug and Cosmetic Act was passed in 1938, the AMA's House of Delegates adopted a resolution which pledged support toward the formation and enactment of effective food and drug legislation focused on protection of the people.

More progress was forthcoming when, in June 1967, an official agreement on a program for the selection of nonproprietary names for drugs was signed between the sponsors of the USAN Council and the FDA. The original USAN Council sponsors were the AMA, the American Pharmacist's Association (APhA) and the United States Pharmacopeial Convention (USP). This agreement stipulated that the FDA would accept as the "official or established" name any drug name the USAN Council adopted. According to this agreement, the Commissioner of the FDA reserved the right to select the official name if the USAN Council could not reach a consensus. The designation of a name as an "official or established" name by the FDA did not follow automatically but was accomplished by publication, subject to public comment, in the Federal Register. All parties upheld this agreement until it was modified 17 years later. In 1984 an amendment to the Food, Drug & Cosmetics Act stated in part that "interested persons, in the absence of the designation of an official name, may rely on the USAN listed in USAN and the USP Dictionary of Drug Names as being the established name in accordance with the Federal Food, Drug and Cosmetic Act." (Federal Register Vol. 49, No. 187).

Upcoming Events

- ✓ 67th INN Fall Consultation – October 23-26th, 2018
- ✓ USAN Council Winter Meeting – January 18th, 2019

About USAN

The purpose of the United States Adopted Names (USAN) Council is to serve the health professions of the United States by selecting simple, informative and unique nonproprietary names for drugs by establishing logical nomenclature classifications based on pharmacological and/or chemical relationships.

The USAN Council is tri-sponsored by the American Medical Association (AMA), the United States Pharmacopeial Convention (USP) and the American Pharmacists Association (APhA). The USAN Council aims for global standardization and unification of drug nomenclature and related rules to ensure that drug information is communicated accurately and unambiguously. It works closely with the International Nonproprietary Name (INN) Program of the World Health Organization (WHO) and various national nomenclature groups.

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