Monoclonal Antibodies

In October 2008, the International Nonproprietary Name (INN) Working Group Meeting on Nomenclature for Monoclonal Antibodies (mAb) met to review and streamline the monoclonal antibody nomenclature scheme. Based on the group's recommendations and further discussions, the INN Experts published changes to the monoclonal antibody nomenclature scheme.

In 2011, the INN Experts published an updated "International Nonproprietary Names (INN) for Biological and Biotechnological Substances—A Review" (PDF) with revisions to the monoclonal antibody nomenclature scheme language.

The USAN Council has modified its own scheme to facilitate international harmonization. This page outlines the updated scheme and supersedes previous schemes. It also explains policies regarding post-translational modifications and the use of 2-word names.

The council has no plans to retroactively change names already coined. They believe that changing names of monoclonal antibodies would confuse physicians, other health care professionals and patients.

Manufacturers should be aware that nomenclature practices are continually evolving. Consequently, further updates may occur any time the council believes changes are necessary. Changes to the monoclonal antibody nomenclature scheme, however, should be carefully considered and implemented only when necessary.

Elements of a Name

The suffix "-mab" is used for monoclonal antibodies, antibody fragments and radiolabeled antibodies. For polyclonal mixtures of antibodies, "-pab" is used. The

-pab suffix applies to polyclonal pools of recombinant monoclonal antibodies, as opposed to polyclonal antibody preparations isolated from blood. It differentiates polyclonal antibodies from individual monoclonal antibodies named with -mab.

Sequence of Stems and Infixes

The order for combining the key elements of a monoclonal antibody name is as follows:

1. Prefix
2. Infix representing the target or disease
3. Infix indicating the source
4. Stem used as a suffix

Prefix

To create a unique name, a distinct, compatible syllable or syllables should be selected as the starting prefix.

Suggested prefixes should comply with the USAN Program's **rules for coining names**. In addition, we ask that manufacturers watch for potential conflicts with names of other monoclonal antibodies, because approximately 200 monoclonal antibodies have already been named. Although it is desirable that names be as short as possible, a prefix that is 2 or more syllables long may be necessary to distinguish the name from those previously assigned.

Target/Disease Class Infix

The general disease state subclass must be incorporated into the name. This is accomplished with the target/disease class infix. The USAN Council has approved specific syllables to denote diseases or targets. Additional subclasses may be added as necessary.

The choice of infix is determined by the available information regarding initial clinical indications and antibody action. The council may request more details and evidence regarding antibody action and indications if necessary.

The target/disease infix has been truncated to a single letter when the source infix begins with a vowel. Using a single letter can create problems with pronunciation, such as with humanized and chimeric antibodies. Therefore a second letter—a

vowel—is added. The infixes that refer to the disease or target class are shown in the table.

Target/Disease Class Infixes for Monoclonal Antibodies (Infix, Definition and Example Suffixes as Used):

Infix: -tu-/-t-
Definition: tumors
Example: -tuzumab/-tumab/-tomab

Infix: -li-/-l-
Definition: immunomodulator
Example: -liximab/-lumab/-lixizumab

Infix: -ba-/-b-
Definition: bacterial
Example: -bixumab/-bumab

Infix: -ci-/-c-
Definition: cardiovascular
Example: -cixumab/-cumab

Infix: -fu-/-f-
Definition: antifungal
example: -fuzumab/-fumab

infix: -gr(o)-
Definition: skeletal muscle mass related growth factors and receptors as target
Example: -grumab

Infix: -ki-/-k-
Definition: interleukins
Example: -kiximab/-kumab

Infix: -ne-/-n-
Definition: neurons as targets
Example: -nezumab/-numab

Infix: -so-/-s-
Definition: bone
Example: -somab/-sumab

Infix: -vi-/-v-
Definition: viruses, antiviral indications
Example: -vizumab/-vumab

The tumor-specific infixes have been discontinued because most monoclonal antibodies with oncology indications are investigated for more than 1 type of tumor. Thus, the following infixes are no longer used: -col- (colon cancer), -mel- (melanoma), -got- (testes), -gov- (ovarian), and -po- (prostate).

Source Infix

Identification of the "source" of the antibody is an important safety consideration, as some products may cause source-specific antibodies to develop in patients. Because an antibody may be based on the sequence of one species but manufactured in cell lines derived from another, "source" is defined as referring to the species on which the immunoglobulin sequence of the mAb is based. This definition harmonizes with that used by the INN Program.

A series of infixes which immediately precede -mab or -pab indicate the source. A limited subset of infixes used most often accounts for nearly all the monoclonal antibody names.

The distinction between chimeric and humanized antibodies is as follows:

Chimeric: A chimeric antibody is one for which both chain types are chimeric as a result of antibody engineering. A chimeric chain is a chain that contains a foreign variable domain (originating from 1 species other than human, or synthetic or engineered from any species including human) linked to a constant region of human origin. The variable domain of a chimeric chain has a V region amino acid sequence which, when analyzed as a whole, is closer to nonhuman species than to human.

Humanized: A humanized antibody is one for which both chain types are humanized as a result of antibody engineering. A humanized chain is typically a chain in which the complementarity determining regions (CDR) of the variable domains are foreign (originating from 1 species other than human, or synthetic) whereas the remainder of the chain is of human origin. Humanization assessment is based on the resulting amino acid sequence, and not on the methodology itself, which allows protocols other than grafting to be used. The variable domain of a humanized chain has a V region amino acid sequence which, when analyzed as a whole, is closer to human than to other species.

New Monoclonal Antibody Rules (PDF)

Source Infixes Used Frequently

Infix: -zu-
Definition: humanized

Infix: -o-
Definition: mouse

Infix: -u-
Definition: fully human

Infix: -xi-
Definition: chimeric

Infix: -xizu-
Definition: combination of humanized and chimeric chains

Source Infixes Used Seldom

Infix: -axo-
Definition: rat/mouse chimer

Infix: -e-
Definition: hamster

Infix: -a-
Definition: rat

Infix: -i-
Definition: primate

USAN Modified Designations for Monoclonal Antibodies

In several instances, the name of a monoclonal antibody incorporates additional clarifying words.

If the antibody is conjugated to a payload—such as radiolabel or toxin, this conjugate is identified by using a separate, second word or other acceptable chemical designation. For monoclonals conjugated to a toxin, the "-tox" stem must be included as part of the name selected for the toxin (e.g., zolimomab aritox, in

which aritox identifies ricin A-chain). In other cases (e.g., brentuximab vedotin) the payload may receive a name based on a stem or a chemical name.

For radiolabeled products, the word order is

1. Name of the isotope
2. Element symbol
3. Isotope number
4. Name of the monoclonal antibody, as follows:

-technetium Tc 99m biciromab
-indium In 111 altumomab pentetate

The peg- prefix may be used for pegylated mAbs, but it should be avoided if it leads to an overly long name. Usually a 2-word name is preferable with the first word referring to the monoclonal antibody and "pegol" as the second word.

When firms apply to name an antibody conjugated to a payload, they should file separate USAN applications for the antibody and the payload, as well as the application for the conjugate. This allows the USAN Council to assign separate USAN designations to each component. The **USAN Modified Application** may be used for the additional names.

USAN Requirements for Monoclonal Antibodies

When naming Monoclonal Antibodies the following items are required to be submitted with your application materials:

- Complete mature amino acid sequence in a **Microsoft Word document**
- 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; 85%+ -zumab or -umab, <85% -ximab)

- 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)