What’s in a Name – Nomenclature of Monoclonal Antibodies
Things you get after 20 mins:

1. How drugs are named
2. Monoclonal antibodies (mAb) as an example:
   A. How to know a mAb by its name
   B. How to correlate the pharmacological properties to a mAb you know nothing but the name only
HOW DRUGS ARE NAMED
How drugs are named

• Mainly by two organizations:

✓ WHO’s International Nonproprietary Names (INN)

✓ United States Adopted Names (USAN)
International Nonproprietary Names

Guidance
International Nonproprietary Names (INN) facilitate the identification of pharmaceutical substances or active pharmaceutical ingredients. Each INN is a unique name that is globally recognized and is public property. A nonproprietary name is also known as a generic name.

General guidance

Mandate
WHO has a constitutional mandate to "develop, establish and promote international standards with respect to biological, pharmaceutical and similar products". The World Health Organization collaborates closely with INN experts and national nomenclature committees to select a single name of worldwide acceptability for each active substance that is to be marketed as a pharmaceutical. To avoid confusion, which could jeopardize the safety of patients, trade-marks should neither be derived from INNs nor contain common stems used in INNs. The selection and publication of INNs falls under the responsibility of the HSS/EMP/QSM team of the INN Programme.

Information

INN consultations and meetings

Requesting an INN

Selection process of INNs
Full text

To apply for a new INN, please use the online application form

LATEST NEWS

55th INN consultation
The 55th Consultation on International Nonproprietary Names (INN) for Pharmaceutical Substances will take place from: 16-18 October 2012.

Deadlines for submissions:
New INN requests
Thursday, 16 August 2012.

Outstanding INN requests
Thursday, 9 August 2012.
Early submissions are encouraged and welcome.

ONLINE APPLICATIONS IS COMPULSORY, please click here...  
INN consultations and meetings

Open Sessions with INN stakeholders
(on 16th October 2012)
Deadline 9 August 2012
Read more...

Training course on INN - 2013
Date to be confirmed
Request for an international nonproprietary name (INN)
Demande de dénomination commune internationale (DCI)

Fee: US$ 9000 (for details see overleaf)

For completion by WHO
A remplir par l’OMS

Request No:
Date:
Copies forwarded:
Date:
Payment received:
Date of cheque:
Acknowledged:

We hereby request the World Health Organization to establish a free and unrestricted INN for the pharmaceutical substance described below.

L’OMS est priée de bien vouloir établir une DCI à usage libre pour la substance pharmaceutique en question.

SUGGESTED NAMES (in order of preference):
DENOMINATIONS PROPOSEES (par ordre de préférence)

1. First suggested name
2. Second suggested name
3. Third suggested name
4. Fourth suggested name
5. Fifth suggested name
6. Sixth suggested name

Biological

CHEMICAL NAME OR DESCRIPTION (INCLUDING STEREOCHEMICAL INFORMATION):
NOM OU DESCRIPTION CHIMIQUE (Y COMPRIS L’INFORMATION SUR LA STÉRÉOCHIMIE)

Chemical Name

GRAPHIC FORMULA (INCLUDING AMINO ACID OR DNA SEQUENCES IN ELECTRONIC FORMAT):
FORMULE GRAPHIQUE (Y COMPRIS LES SEQUENCES D’ACIDES AMINES OU D’ADN EN FORMAT ELECTRONIQUE):

Add BMP Structure Image
United States Adopted Names

The purpose of the United States Adopted Names Council (USANC) is to serve the health professions in 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 USANC is tri-sponsored by the American Medical Association (AMA), the United States Pharmacopeial Convention (USP), and the American Pharmacists Association (APhA). In addition, the Food and Drug Administration (FDA) cooperates with and is represented on the USANC. The USANC aims for global standardization and unification of drug nomenclature and related rules to ensure that drug information is communicated accurately and unambiguously. The USANC works closely with the International Nonproprietary Name (INN) Program of the World Health Organization (WHO), and various national nomenclature groups.

Adopted names
A listing of adopted USAN.

USAN application process: how to apply for a name
Considerations and requirements before, during and after a name is recommended and adopted.

Names under consideration
A listing of names under consideration by the USAN Council.

Naming biologics
Guidelines for assigning USAN for biological products such as insulins, interferons, interleukins, growth hormones, colony-stimulating factors, cytokines, monoclonal antibodies, and other pharmaceutical products.
Is a USAN required for my substance?

If a firm plans to market a therapeutic substance in the United States (US) and the USAN Council (USANC) names this type of therapy, a USAN should be requested. It is USAN policy that US pharmaceutical companies who intend to market their product(s) in the US, first apply for a nonproprietary name through their national nonproprietary naming commission, which in the US is the USAN Program. An International Nonproprietary Name (INN) is not a substitute for a USAN. In requesting a USAN, the sponsor gives permission to involve the INN Expert Group in creating a global name. After the USANC and the sponsor agree on a name, the USANC Secretariat submits it to the INN Expert Group for consideration, additional trademark clearance and linguistic evaluation. Because of the global nature of nonproprietary names and with so many pharmaceutical companies being multinational, a single designation used worldwide serving as the nonproprietary name in the US and in other countries is beneficial. If the name submitted to the USANC was previously approved by the INN Expert Group, indicate the WHO request number and/or proposed/recommended INN (pINN/rINN) list numbers on the USAN application. Firms that have an INN must apply for a USAN if they intend to use the name in the US.
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<td>Joshua</td>
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<td>Jack</td>
<td>Addison</td>
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<td>Logan</td>
<td>Hailey</td>
<td>James</td>
</tr>
<tr>
<td>10</td>
<td>Matthew</td>
<td>Lily</td>
<td>William</td>
</tr>
</tbody>
</table>
The use of stems in the selection of International Nonproprietary Names (INN) for pharmaceutical substances

2011
PART II B

ALPHABETICAL LIST OF COMMON STEMS AND THEIR DEFINITION

A

-abine (see -arabine and -citabine)  arabinofuranosyl derivatives; nucleoside antiviral or antineoplastic agents, cytarabine or azactidine derivatives

-ac  anti-inflammatory agents, ibufenac derivatives

-acetam (see -racetam)  amide type nootropic agents, piracetam derivatives

-actide  synthetic polypeptide with a corticotropin-like action

-adol/-adol-  analgesics

-adom  analgesics, tifluadom derivatives

-afenone  antiarrhythmics, propafenone derivatives

-afil  inhibitors of phosphodiesterase PDE5 with vasodilator action

-aj-  antiarrhythmics, ajmaline derivatives
ANNEX 2

GENERAL PRINCIPLES FOR GUIDANCE IN DEVISING INTERNATIONAL NONPROPRIETARY NAMES FOR PHARMACEUTICAL SUBSTANCES*

1. International Nonproprietary Names (INN) should be distinctive in sound and spelling. They should not be inconveniently long and should not be liable to confusion with names in common use.

2. The INN for a substance belonging to a group of pharmacologically related substances should, where appropriate, show this relationship. Names that are likely to convey to a patient an anatomical, physiological, pathological or therapeutic suggestion should be avoided.

These primary principles are to be implemented by using the following secondary principles:

3. In devising the INN of the first substance in a new pharmacological group, consideration should be given to the possibility of devising suitable INN for related substances, belonging to the new group.

4. In devising INN for acids, one-word names are preferred; their salts should be named without modifying the acid name, e.g. "oxacillin" and "oxacillin sodium", "ibufenac" and "ibufenac sodium".

5. INN for substances which are used as salts should in general apply to the active base or the active acid. Names for different salts or esters of the same active substance should differ only in respect of the name of the inactive acid or the inactive base.

For quaternary ammonium substances, the cation and anion should be named appropriately as separate components of a quaternary substance and not in the amine-salt style.
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For quaternary ammonium substances, the cation and anion should be named appropriately as separate components of a quaternary substance and not in the amine-salt style.

6. The use of an isolated letter or number should be avoided; hyphenated construction is also undesirable.

7. To facilitate the translation and pronunciation of INN, “f” should be used instead of “ph”, “t” instead of “th”, “e” instead of “ae” or “oe”, and “i” instead of “y”; the use of the letters “h” and “k” should be avoided.

8. Provided that the names suggested are in accordance with these principles, names proposed by the person discovering or first developing and marketing a pharmaceutical preparation, or names already officially in use in any country, should receive preferential consideration.

9. Group relationship in INN (see Guiding Principle 2) should if possible be shown by using a common stem. The following list contains examples of stems for groups of substances, particularly for new groups. There are many other stems in active use. Where a stem is shown without any hyphens it may be used anywhere in the name.
When there are updates...
Addendum¹ 1 to

"The use of stems in the selection of International Nonproprietary names (INN) for pharmaceutical substances"

WHO/EMP/QSM/2011.3
Addendum\(^1\) 1 to "The use of stems in the selection of International Nonproprietary Names (INN) for pharmaceutical substances" - WHO/EMP/QSM/2011.3

\(^1\) This addendum is a cumulative list of all new stems selected by the INN Expert Group since the publication of "The use of stems in the selection of International Nonproprietary Names (INN) for pharmaceutical substances" 2011.

- tibant  
  bradykinin receptor antagonists
  anatibant (88), deltibant (75), fasitibant chloride (103), icatibant (67), safotibant (105)

- zomib  
  proteasome inhibitors
  bortezomib (88), carfilzomib (97), delanzomib (105), ixazomib (104), marizomib (102)
HOW MONOCLONAL ANTIBODIES ARE NAMED
Focusing on mAbs: Background

* An **antibody** (Ab), also known as an **immunoglobulin** (Ig), is a large Y-shaped protein produced by B-cells

* identify and neutralize foreign objects such as bacteria and viruses
OLD DAYS...
Initially, murine antibodies were obtained by hybridoma technology

- The dissimilarity between murine and human immune systems led to the clinical failure of these antibodies
- Major problems included reduced stimulation of cytotoxicity and the formation of complexes after repeated administration, which resulted in mild allergic reactions and sometimes anaphylactic shock.
To reduce murine antibody immunogenicity, murine molecules were engineered to remove immunogenic content and to increase their immunologic efficiency initially achieved by the production of chimeric and humanized antibodies.
Chimeric

- murine variable regions fused onto human constant regions
- This reduces immunogenicity, and thus increases serum half-life.
Humanized

* grafting murine amino acid domains into human antibodies
* ~95% human origin
Human

* transferring human immunoglobulin genes into the murine genome
* Then the transgenic mouse is vaccinated against the desired antigen, leading to the production of monoclonal antibodies
International Nonproprietary Names (INN) Working Group Meeting on Nomenclature for Monoclonal Antibodies (mAb)
Geneva, 6-7 October 2008

Meeting Report

Programme on International Nonproprietary Names (INN)
International Nonproprietary Names (INN) for biological and biotechnological substances (a review)
Components of the mAb names:

* Prefix
* Sub-stem A
* Sub-stem B
* Suffix
* (Second word)
-mab, for all products containing an immunoglobulin variable domain which binds to a defined target
Substem B

* Indicated the **species** on which the immunoglobulin sequence of the mAb is based

<table>
<thead>
<tr>
<th>Substem B (for the species)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>$a$</td>
<td>rat</td>
</tr>
<tr>
<td>$axo$ (pre-sub-stem)</td>
<td>rat/mouse</td>
</tr>
<tr>
<td>$e$</td>
<td>hamster</td>
</tr>
<tr>
<td>$i$</td>
<td>primate</td>
</tr>
<tr>
<td>$o$</td>
<td>mouse</td>
</tr>
<tr>
<td>$u$</td>
<td>human</td>
</tr>
<tr>
<td>$xi$</td>
<td>chimeric</td>
</tr>
<tr>
<td>-xizu-</td>
<td>chimeric-humanized</td>
</tr>
<tr>
<td>$zu$</td>
<td>humanized</td>
</tr>
</tbody>
</table>
Table 2 Substem B for the species

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>$a$</td>
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<tr>
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<td>primate</td>
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<td>$o$</td>
<td>mouse</td>
</tr>
<tr>
<td>$u$</td>
<td>human</td>
</tr>
<tr>
<td>$xi$</td>
<td>chimeric</td>
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<tr>
<td>-$xizu$-</td>
<td>chimeric-humanized</td>
</tr>
<tr>
<td>$zu$</td>
<td>humanized</td>
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</tbody>
</table>
Substem A

* Indicates the **targets** (molecule, cell, organ, system) of the mAbs

<table>
<thead>
<tr>
<th>Substem A</th>
<th>Description</th>
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<tbody>
<tr>
<td>-b(a)-</td>
<td>bacterial</td>
</tr>
<tr>
<td>-c(i)-</td>
<td>cardiovascular</td>
</tr>
<tr>
<td>-f(u)-</td>
<td>fungal</td>
</tr>
<tr>
<td>-k(i)-</td>
<td>interleukin</td>
</tr>
<tr>
<td>-l(i)-</td>
<td>immunomodulating</td>
</tr>
<tr>
<td>-n(e)- (under discussion)</td>
<td>neural</td>
</tr>
<tr>
<td>-s(o)-</td>
<td>bone</td>
</tr>
<tr>
<td>-tox(a)-</td>
<td>toxin</td>
</tr>
<tr>
<td>-t(u)-</td>
<td>tumour</td>
</tr>
<tr>
<td>-v(i)-</td>
<td>viral</td>
</tr>
</tbody>
</table>

In principle, a single letter, e.g. -b- for bacterial is used as substem A. Whenever substem B starts with a consonant (e.g. x or z), to avoid problems in pronunciation, an additional vowel indicated in the table, e.g. -ba- is inserted.
Table 3 Substem A for target class

<table>
<thead>
<tr>
<th>Substem</th>
<th>Category</th>
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<tbody>
<tr>
<td>-b(a)-</td>
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<tr>
<td>-c(i)-</td>
<td>cardiovascular</td>
</tr>
<tr>
<td>-f(u)-</td>
<td>fungal</td>
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<tr>
<td>-k(i)-</td>
<td>interleukin</td>
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* Bracket letter is used when Substem A is a consonant and meets another consonant with Substem B, e.g.:
  * Golimumumab
  * Golmumumab
<table>
<thead>
<tr>
<th>Prefix</th>
<th>Target substem</th>
<th>Source substem</th>
<th>Stem</th>
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<td></td>
<td>old</td>
<td>new</td>
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</tr>
<tr>
<td>variable</td>
<td>-anibi-</td>
<td>—</td>
<td>angiogenesis (inhibitor)</td>
</tr>
<tr>
<td></td>
<td>-ba(c)-</td>
<td>-b(a)-</td>
<td>bacterium</td>
</tr>
<tr>
<td></td>
<td>-ci(r)-</td>
<td>-c(i)-</td>
<td>circulatory system</td>
</tr>
<tr>
<td></td>
<td>-fung-</td>
<td>-f(u)-</td>
<td>fungus</td>
</tr>
<tr>
<td></td>
<td>-ki(n)-</td>
<td>-k(i)-</td>
<td>interleukin</td>
</tr>
<tr>
<td></td>
<td>-les-</td>
<td>—</td>
<td>inflammatory lesions</td>
</tr>
<tr>
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<td>-li(m)-</td>
<td>-l(i)-</td>
<td>immune system</td>
</tr>
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<td></td>
<td>-mul-</td>
<td>—</td>
<td>musculoskeletal system</td>
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<tr>
<td></td>
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<td>-n(e)-</td>
<td>nervous system</td>
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<td>bone</td>
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<td>-toxa-</td>
<td>-tox(a)-</td>
<td>toxin</td>
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<td>-co(l)-</td>
<td>-t(u)-</td>
<td>colonic tumor</td>
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<tr>
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<td>—</td>
<td>ovarian tumor</td>
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<td>—</td>
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<td>—</td>
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<td>-pr(o)-</td>
<td>—</td>
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<td></td>
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</tr>
<tr>
<td></td>
<td>-vi(r)-</td>
<td>-v(i)-</td>
<td>virus</td>
</tr>
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</table>
Random, just to give a distinctive and well sounding name

mAbs with the same source and targeting the same substems are only distinguished by their prefixes.
If the monoclonal antibody is conjugated to another protein or to a chemical (e.g. chelator), identification of this conjugate is accomplished by use of a separate, second word or acceptable chemical designation.
A cytotoxic agent can be linked to an anti-tumor antibody for drug targeting purposes.

The word *vedotin*, for example, stands for monomethyl auristatin E which is toxic by itself but predominantly affects cancer cells if used in conjugates like:

- glembatumumab vedotin
An antibody can be PEGylated (attached to molecules of polyethylene glycol) to slow down its degradation by enzymes and to decrease its immunogenicity.

The prefix *peg-* can be used for pegylated mAbs, but this should be avoided if it leads to over-long INN.

In most cases, it is best to adopt **two-word INN for pegylated mAbs**, with the first word describing the mAb and the second being *pegol* or a related designation.

E.g. *alacizumab pegol*
If the monoclonal antibody is radiolabelled, the radioisotope is listed first in the INN

e.g.

*technetium (\(^{99m}\)Tc) nofetumomab merpentan*
Exercise:

- Olaratumab
- Benralizumab
- Palivizumab
- Abciximab
- Denosumab
- Ranibizumab
- Adalimumab
- Muromomab CD$_3$
* Olaratumab

* Olara-t-u-mab

human monoclonal antibody acting against tumors
Benralizumab

Benra-li-zu-mab

humanized monoclonal antibody acting on the immune system
Palivizumab

Pa-li-vi-zu-mab

humanized monoclonal antibody acting on the immune system and against virus

→ Prevention of RSV
Abciximab

Ab-ci-xi-mab

chimeric monoclonal antibody used on the cardiovascular system

→ Binds to IIb/IIIa receptors, inhibits platelet aggregation
* Denosumab

* Deno-s-u-mab

human monoclonal antibody used on the bones

→ Osteoporosis
Ranibizumab

- **R-anibi-zu-mab**

  humanized monoclonal antibody as well as an inhibitor of angiogenesis

  → Targeting VEGF-A, for Aged related macular degeneration
Special cases:

* Adalimumab

* Adalumab
  (if named after 2009 update of target substem)

<table>
<thead>
<tr>
<th>Prefix</th>
<th>old</th>
<th>new</th>
<th>meaning</th>
</tr>
</thead>
<tbody>
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<td>variable</td>
<td>-anibi-</td>
<td>—</td>
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<td></td>
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<tr>
<td>-ci(r)-</td>
<td>-c(i)-</td>
<td></td>
<td>circulatory system</td>
</tr>
<tr>
<td>-fung-</td>
<td>-f(u)-</td>
<td></td>
<td>fungus</td>
</tr>
<tr>
<td>-ki(n)-</td>
<td>-k(i)-</td>
<td></td>
<td>interleukin</td>
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<td>-les-</td>
<td>—</td>
<td></td>
<td>inflammatory lesions</td>
</tr>
<tr>
<td>-li(m)-</td>
<td>-l(i)-</td>
<td></td>
<td>immune system</td>
</tr>
</tbody>
</table>
Muromomab CD$_3$

* depletes circulating T cells and prevents organ graft rejection
Muromomab CD$_3$

* **Murine monoclonal antibody** targeting CD$_3$.
* Why the naming convention is so different?
  * Muromomab CD3 first approved for clinical use in human in 1986
  * The INN stem –*mab* proposed for naming monoclonal antibodies after 1990