What's In a Drug Name?

A rose might smell as sweet by any other name, but the process of naming the growing number of medications has become quite complex and serious.

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Peter Pepper, PharmD, prepares parenteral parecoxib, piloting this pain preparation. Suki Sellars, summer student, shelves celecoxib and Celexa, serendipitously seeing sound similarities. Xavier Xerin, tech extraordinaire, expounds extemporaneously, "Xanax, Xigris, Zaditor, zidovudine, zileuton, zoledronate. What's with all the *x*'s and *z*'s?" Adrian Arlester, the pharmacist, eyes averted, only articulates, "Ada-lim-, adalim, ad … a … lim … MOO … mab?"

Tongue twisters aside, proprietary (brand names and trademarks) and nonproprietary (generic names) drug lexicon is no game. With more than 33,000 trademarked names and 9,000 generic names in use in the United States,[1] it's no surprise that 15% of all reported errors between 1995 and 2000 resulted from some type of name confusion.[2] Some experts find generic names more confusing than brand names. Consider this: The most common generic names (35% of them) end in *-ne*, averaging 14.4 letters and 5 syllables. The most common proprietary ending (*-in*) is shared by only 5% of proprietary names, which average 10.4 letters and 3.53 syllables.[3] Experts caution about chemical names that "blind us with science"[4] and contain numbers that can be confused with doses or strengths.[3]

In short, the problem is familiar. What's the solution?

Understanding how standard nomenclature manages complexity and minimizes errors is a start.[1] The lesson from psycholinguists is clear: the frequency with which a word appears in print or is spoken enhances word recognition.[5]

Understanding the Lingo: Generic Names

The solution starts with understanding the lingo, which for generics has been determined by the United States Adopted Names (USAN) Council since 1961. Although its offices are in the American Medical Association's headquarters in Chicago, the USAN Council also includes representation from the American Pharmacists Association (APhA), and the United States Pharmacopeial Convention (USPC). A Food and Drug Administration (FDA) liaison also participates in USAN deliberations. The Council's selection criteria are actually quite organized, and the organization strives for usefulness, defined as suitability of names in routine, clinical, educational, and international use.

Although a drug or biologic agent's sponsor asks for a generic name and may suggest one, the name does not become the sponsor's property once approved.[3] The USAN Council isn't the last word for generic name selection. To facilitate international harmony, USAN choices must be approved by the World Health Organization's International Nonproprietary Name Committee.[3,6]

The USAN Council has rules, some firm and some unwritten. Key is this: People rely on first several letters to differentiate similar names. This may be why stems at the front of the name, like the *cep-* that plagued the cephalosporin class, are no longer used. Some other current naming conventions are listed in Table 1.

Drug sponsors sometimes suggest names that the USAN considers inappropriate. In that case, USAN suggests new names. Twice a year, the International Nonproprietary Name Committee reviews all proposed names. Approximately 60% of new names emanate from the prolific drug industry in the United States. Some of the problems with naming are understandably complex. A name chosen in one country may already be a word in another country, or it may incorporate an offensive slang term unknown to the naming party. Over the years, members of the committee accumulate incredible institutional knowledge about what probably will be rejected by people from other cultures who speak different languages.[6]

USANs: Straightforward?

The USAN (in this case meaning the generic or nonproprietary name) should be short, easy to pronounce, and euphonic. Misleading or confusing sounds or syllables are also undesirable.

Table 1. Select USAN Naming Considerations

Rule	Reason
The prefix *rac-* is restricted.	This implies racemic and can only be used for a racemic mixture.
Dex- and *lev-* are restricted.	Only dextro- [*R*(+)] or levo- [*S*(–)] rotating enantiomers can carry these prefixes.
Ar- and *es-* are restricted.	These are reserved for the *R*(-) and *S*(+) isomers of the levorotatory and dextrorotatory forms, respectively.
Generics do not begin with the letters *H, J, K,* or *W.*	These letters either do not exist in some of the 130 countries that use USANs, or have different sounds in various languages.
There is a moratorium on the use of *X* and *Z* as lead letters on generic names.	This is a euphonics issue: *X* and *Z* often sound alike at the start of words.
USAN avoid prefixes and stems like *brev, vel, mal,* or *mor.*	These stems either have or imply other things (brevity, velocity, bad, or death, respectively).
USAN should not be selected based on a drug or agent's target indication.	Indications often change; mechanism of action is a better basis for names.

Names are based on stems, which are letter sequences common to a group of drugs that share pharmacologic actions. So, the stem *-coxib* refers to a selective COX-1 inhibitor, just as the stem *-erg-* refers to ergot alkaloids. The stems are not secret; a list is available at www.ama-assn.org/go/usan.

Monoclonal Antibodies: Difficult

Today, the monoclonal antibodies (MABs) pose one of the greatest challenges to the people responsible for creating and approving drug names. It's difficult to keep their names simple, informative, and unique, and the problem has led to their tongue-twisting, five- and six-syllable names. Understand how USAN bestows names, and the differences between adalimumab, infliximab, rituximab, and trastuzumab become crystal clear.

A brief review of monoclonal antibody nomenclature can help clinicians pronounce the names and determine the MAB's source and purpose.

All monoclonal antibodies and fragments end with the suffix *-mab*. Many of them are of animal origin, and this is an important safety factor because many products may cause source-specific antibodies to develop in patients. USAN clues clinicians about this potential through use of source identifiers that precede the *-mab* suffix stem (see Table 2). The general disease state subclasses are incorporated into the name by use of a code syllable. Additional subclasses will certainly be necessary, and USAN will add them as appropriate. More information about MAB nomenclature and that of other biolo*gicals* is available on the USAN's Web site (www.ama-assn.org/go/usan).

As illustrated in Table 2, infliximab is an immunomodulating chimeric monoclonal antibody, adalimumab is an immunomodulating humanized monoclonal antibody, rituximab is a chimeric monoclonal antibody, and trastuzumab is a humanized monoclonal antibody, with the last two agents used in tumors.

The USAN Web site also offers specialized pages offering similar explanations for erythropoietins, interferons, interleukins, and somatotropins.

Brand Names and Trademarks

As drugs and biologics are being developed, marketers work behind the scenes searching for a unique brand name in a process that is estimated to cost up to $2.25 million.[2] Why? The drug's sponsor (manufacturer or parent company) must conduct searches to avoid using an inappropriate or already claimed name, and often their research involves investigations in up to 130 countries.[2]

Brand-name screening and approval is the FDA's domain, and it prohibits names associated with the product's intended indication. Further, FDA staff members disallow names that imply efficacy. Simply put, the name shouldn't mean anything.[7] Unlike the USAN Council (which will suggest alternatives for names deemed inappropriate), the FDA flatly rejects fully one third of the hundreds of names proposed annually without offering alternatives. Manufacturers faced with rejection must develop a new name on their own.[3,8]

Into the 1970s, sponsors preferred drug names that began with the letter *A* so physicians scanning formularies or drug lists would see their products first. Companies also asked employees for suggestions.[7,9] Today's competitive environment, fueled by direct-to-consumer advertising and safety concerns, is markedly different. Marketers look for names that subtly and indirectly convey an idea, suggesting improved quality of life rather than scientific origin. Considering that drug names are conjured from thin air, cannot have stand-alone meaning, and have a good probability of FDA rejection, most marketers select several names for testing.

From Functional to Fricative

Marketers veer away from traditional functional names that are simply built on the company's or inventor's name. Today's brand names are invented, experiential, or evocative. Developers might look for anagrams (words made from transposed letters of another word, like Halcion), or palindromes (words spelled the same backward and forward).[10] More than likely, plosives will be employed.

Table 2. Stem Derivation as Applied to Monoclonal Antibodies

Derivation	Examples
1. Identify the monoclonal antibody or fragment using the suffix *–mab*.	Inflixi**mab** Adalimu**mab** Rituxi**mab** Trastuzu**mab**
2. Identify the animal source: *a* = rat; *e* = hamster; *i* = primate; *o* = mouse; *u* = human; *xi* = chimera (from proteins or genes of two different species); *zu* = humanized.	Infl**ixi**mab Adalim**u**mab Ritu**xi**mab Trastu**zu**mab
3. Identify the target disease or condition: viral = *-vir-*; bacterial = *-bac-*; immune (immunomodulator)= *-lim-*; infectious lesions = *-les-*; cardiovascular = *-cir-*; tumor = *-tu-*.	Inf**li**ximab Ada**lim**umab Ri**tu**ximab Tras**tu**zumab

Certain letters (*P*, *T*, *D*, *K*, *Q*, and hard *C*) give the name a strong sound that causes it to explode forcefully from the mouth. Studies have shown these letters are the most effective for marketing purposes, which is why the most common first two-letter combination in drug names is *pr*.[10–12] In addition, drug names are peppered with fricatives—letters like *X* and *Z* that sound fast.[10,12] (Does Ex-Lax sound fast to you?[12]) Marketers like the soft *C*, *S*, and *L* letters for lifestyle products.

Once a few names are selected, marketing researchers engage hundreds of paid volunteers. Prescribers write mock prescriptions so graphologists can analyze the potential for confusion. Experts listen to the way people from various areas pronounce the names. Clinicians and patients are asked to rate names for tonal quality and the impression they leave.[7]

Suggesting Quality of Life

Medications used to treat erectile dysfunction have attracted unprecedented attention, and their sponsors have gone to great lengths to find names that obliterate the stigma associated with this disorder.[9] Marketing literature applauds Pfizer's selection of Viagra (sildenafil citrate) for its suggestion of vitality and because it rhymes with Niagra, connoting force and endurance.[7] They hail its new competitor, Levitra (vardenafil hydrochloride), for its sound of European elegance (*le* from the French word for *the*, *vitra* suggesting *life*), and its aural similarity to libido.[12] (Its European name, Nuviva, was rejected by FDA.) Most people never knew or have forgotten that the name of Eli Lilly's recently approved erectile dysfunction drug, Cialis (tadalafil), adorned a yacht in the America's cup race.[12,13] Lilly now sponsors the race. Derived from the French word for *sky*, *ciel*, and associated with rigid yacht racing, Cialis implies the sky is the limit. The success of these marketing campaigns is apparent: Pfizer sponsors a Viagra car on the NASCAR circuit, and the New England Patriots professional football team promotes Levitra.[13] Stigma is no longer a serious issue.

The Future

People who bestow drug names have concerns about the future. The USAN Council knows technologically complex drugs such as heat shock proteins and gene therapy vectors will pose new challenges.[6] Safety experts worry that the compendium of drug names is so crowded that sound-alike errors will be more common. Research into the drug lexicon, however, indicates that experts should be able to coin new names without creating dangerous similarities for years to come.[1]

In terms of generic names, fewer names (for now) will start with *x*'s or *z*'s.[6] In brand names, fricatives will continue to be common, and *Q*'s without an accompanying *u* seem to be making a debut.[10] Augmenting language will make an appearance—dosage forms that entice the patient to remember (and hopefully prefer) the trademarked product.[10] Ultimately, frequent use of new generic names will enhance understanding of the drugs' function, and careful use of brand names will avoid errors.

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