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# In pursuit of distinction: The method of the non-proprietary name

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**Abstract** This is an update to a paper that appeared in the very first issue of the *Journal of Generic Medicines* in October 2003. Over the past few years, pharmaceutical manufacturers have started to diversify their portfolios to include generic medicines as a way to maximise their investment in patented drugs. With this dynamic as context, understanding the development and construction of a generic name may be helpful both to the manufacturer of patented drugs who wants to support the perception of distinctiveness among competition, as well as to the generics marketer who wants to leverage the legacy of previously patented drugs. This paper intends to define generic names, explain their purpose and the challenges they pose to manufacturers, provide some guidance on their development, and identify how the non-proprietary name can support marketing opportunities.

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## INTRODUCTION

The tension between brands and generics has not changed much in the past few years: patented prescription drugs and blockbuster brands are still the ultimate goal for pharmaceutical manufacturers; generics are ever more the unwanted reminder of loss of exclusivity and a shrunken profit margin. What has changed, though, has been the increasing attention that generics have gained as a potential way for pharmaceutical manufacturers to maximise their own investment in patented drugs. Companies such as Novartis, through their subsidiary Sandoz,

are proving that diversifying portfolios to include generic medicines can be a winning strategy. With this dynamic as context, understanding the development and construction of a generic name may be helpful both to the manufacturer of patented drugs who wants to support the perception of distinctiveness among competition, as well as to the generics marketer who wants to leverage the legacy of previously patented drugs.

For those who are 'originators', developing the generic name is an opportunity to express a scientific point of difference. For marketers of generic drugs, the generic name is a means to assert similarity to previously patented drugs. Although it is the originator who has the capacity to influence the content and construction of the generic name, it is useful for generics marketers to understand how these names come into being, what are their component parts and what they represent.

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## DEFINING TERMINOLOGY: GENERIC NAMES VS NON-PROPRIETARY NAMES

'Generics' can be a confusing term: a generic *drug* is an unbranded pharmaceutical preparation that is bioequivalent to a branded drug but usually sold at a lower price to compete with their branded counterpart after its patent expires.<sup>1</sup> A generic *name* is simply the nomenclature to describe the active ingredient. Every product, whether branded or unbranded has a generic name. For the sake of clarity and consistency, this paper will proceed with the term 'non-proprietary', which can be used interchangeably with 'generic' to describe terminology that is not protected by law and is available for public use.<sup>2</sup>

## DEFINING THE PURPOSE

Non-proprietary names do not play a large role in branded communications, but they are essential to the scientific community and pharmaceutical industry for a variety of reasons. First, the non-proprietary name identifies a drug's 'active ingredient', which may be available through several sources globally and in combination with other active ingredients under different brand names.<sup>2</sup> For example, the active ingredient, *ibuprofen*, can be found in Wyeth's preparation branded as Advil<sup>®</sup> in the US, or in Astellas' Dolofort in Germany and Austria. Standardising the language of the active ingredient helps physicians and patients alike to recognise similarities and differences among products globally. Also, because non-proprietary names are designed to exist as long as the product(s) they identify,<sup>3</sup> they allow the public to identify the same ingredient regardless of the label under which it is sold, for however long the substance is available.

Secondly, the non-proprietary name serves as a valuable counterpart to brands,<sup>3</sup> providing a 'means of preserving trademark rights to a brand name for the article concerned'.<sup>2</sup> To explain: when a manufacturer discovers a compound which is expected to have some therapeutic benefit, the company may apply

for a patent that provides exclusive selling rights for a period of 20 years.<sup>4</sup> During these years of exclusivity, a manufacturer can create a brand name for its preparation as a vehicle to express its unique standards and values. After patent expiry, others may use the non-proprietary name, but they may never use or resemble the protected trade mark. Without non-proprietary names, it would be difficult for new competition to define its active ingredient other than by referencing the originator's brand name. Therefore, non-proprietary names allow for brands to exist and be successful, despite patent expiry and generic competition. For example, although generic fluoxetine exists, Eli Lilly successfully markets its branded version as Prozac<sup>®</sup>. Although other manufacturers can formulate their own preparations of fluoxetine, none are allowed by law to pattern their identity on the Prozac name or its other brand elements. The Prozac trade mark, therefore, associates the preparation with a distinct source and attaches an underlying guarantee of quality and performance specific to that preparation of the active ingredient.

Thirdly, within the medical community there are significant restrictions on when a brand name may be used. Formularies and many journals necessitate the use of the non-proprietary name instead of trade marks to ensure consistent communication among teachers, students, and medical professionals.<sup>2</sup> Also, in some countries, legislation requires that every brand be clearly identified by its non-proprietary name in promotions; while in others, only the non-proprietary name — not the brand name — may be used.<sup>5</sup>

## NATIONAL VS INTERNATIONAL NON-PROPRIETARY NAMES

At one point, many countries had their own non-proprietary nomenclature systems regulated by their own national agencies or pharmacopoeia. Given independent approaches to naming, sometimes, there could

be differences in the non-proprietary name from one country to the next. For instance, acetaminophen and adrenaline in the US are known as paracetamol and epinephrine in the UK, respectively.

Today, this variance is less likely due to the launch of the International Non-Proprietary Name (INN) program by the World Health Organisation (WHO) in 1950. Member states defined Guidelines for development and a procedure for the selection of recommended INNs, which led to their standardisation and consistency across borders.<sup>6</sup> Furthermore, a commitment by member states in 1993 to protect the use of INNs enabled the WHO both to avoid conflicts among non-proprietary names as well as to limit similarity between non-proprietary names and trade marks.<sup>7</sup> So while national names such as British Approved Names (BAN), Dénominations Communes Françaises (DCF), Japanese Adopted Names (JAN), and United States Adopted Names (USAN) still exist, they are more likely to be identical to the INN.<sup>5</sup>

### **DEVELOPING AN INN THROUGH NATIONAL NOMENCLATURE GROUPS SUCH AS THE USAN COUNCIL**

The USAN Council is a national committee devoted to non-proprietary drug nomenclature in the US. It is comprised of five members: one representing the Food and Drug Administration (FDA), one member-at-large, and three representing three different sponsoring organisations, namely the American Medical Association (AMA), the United States Pharmacopoeial Convention (USP), and the American Pharmacists Association (APhA). These experts review names developed by a small USAN naming group in conjunction with the manufacturers themselves, and approve and advise on name adoption. While it is possible to work directly with the WHO to develop an INN, there are several reasons why it may be more expedient and convenient to work with a national

nomenclature group such as the USAN Council:<sup>8</sup>

- (1) In some countries, a national non-proprietary name is required to market the compound, and sometimes there is a preferred protocol for the manufacturer to obtain the national name prior to the INN. This is the case with the USAN Council and WHO. If a US-based manufacturer first applies to the WHO for an INN, approximately 80 per cent of the time the INN secretariat would refer the manufacturer to the USAN program.
- (2) If one applies for a national non-proprietary name first, that name may stand a better chance of being accepted by the WHO by virtue of having been reviewed by nomenclature professionals prior to submission for an INN. For example, when the USAN Council forwards a name to the WHO, the proposed USAN represents approvals by both the USAN Council and, many times, by the FDA, and is therefore more likely to be appropriately crafted and viable.
- (3) National nomenclature groups often facilitate the submission for an INN. For example, the USAN Secretariat completes all INN paperwork and verification required for the INN process. The manufacturer only has one application to fill out — a USAN application.
- (4) Lastly, because the WHO Expert Panel convenes only twice a year to review proposed INNs,<sup>5</sup> working with national nomenclature groups such as the USAN Council, which reviews names all year round, may allow for greater flexibility from a timing perspective.

### **DEVELOPMENT TIMELINE**

Development time varies, depending on whether one is submitting for an INN or a

national non-proprietary name. For example, the time it takes to obtain a proposed USAN varies depending on the number of iterations between manufacturer and Council. Ms Stephanie Shubat, USAN Program Director, explained that it can take three–five iterations before both the Council and the Manufacturer come to an agreement. But it should be understood that the USAN Council and its naming group is not adversarial in any way. In fact, the USAN naming group is extremely accessible and responsive. ‘It’s an interactive process that requires a lot of communication throughout’, says Ms Shubat.<sup>5</sup> One gets the impression that the development of a USAN is not at all a dictatorial process, but more of a collaborative pursuit of mutual agreement.

Once a proposed USAN is submitted to the WHO for an INN, the approval time depends on the next INN committee meeting. The committee meets twice each year in Geneva to review global submissions. Although the US submits approximately 60 per cent of all non-proprietary candidates, the negotiations are consensus driven and every nation’s registries and concerns are factored equally.<sup>5</sup> Given the number of non-proprietary names that exist in the world, having a non-proprietary name emerge as clear of any obstacle or conflict is an awesome feat.

Within all member states of the WHO, a medical preparation cannot be sold without an established non-proprietary name. Therefore, the non-proprietary name needs to be in place by the time the manufacturer receives the letter of approval from the national regulatory agency, which signals the go-ahead for commercialisation. The process of obtaining a non-proprietary name can begin as soon as the drug enters clinical trials. Ultimately, if developing a USAN first then an INN, it can take approximately 3–8 months for a proposed USAN, while securing an INN can take an additional 6–8 months.<sup>5</sup>

## FACTORS FOR APPROVAL: THE STEM AND UNIQUE IDENTIFICATION

A non-proprietary name must identify the compound’s scientific classification using the appropriate common ‘stem’.<sup>2,6</sup> One can think of the stem as a surname. It represents the chemical and/or structural family to which a compound belongs. Meanwhile, the remainder of the name denotes the ‘family member’. There can be several family members offering different advantages, but their scientific heredity and similarity are conveyed through the stem.

The stem is a letter string about five letters long, on average, but may be as short as two letters or as long as nine. The majority of stems are used in the suffix position, at the end of the name, although some stems are intended for the prefix position and still others as an infix, embedded in the middle of the name. This variation in length and placement can sometimes cause difficulties in accurately constructing a name for submission, but according to Ms Shubat, the most common mistake is that the manufacturer does not use the proper stem to designate its class. Usually, the USAN Council or WHO will correct the stem and suggest ways to reengineer the name to preserve the remaining portion of the original name.<sup>5</sup>

There are instances wherein a compound’s chemistry or structure is so novel that it cannot be categorised into any existing ‘family’. In these cases, a new stem may need to be developed. A new stem can be developed for use as either a prefix, infix or, more frequently, a suffix. A manufacturer can develop and submit new stems for consideration on the basis of unprecedented science. The USAN Council and the WHO will entertain these suggestions pending a review of the compound’s chemistry, structure and mechanism to verify its novelty.<sup>3,5</sup> If the novelty of the science is confirmed, and a new stem is warranted, the new stem will be reviewed and revised to optimise its fit with existing nomenclature.

Every innovation and corresponding new stem has to be catalogued, and it is a

monumental task to create and enforce the codification. Therefore, nomenclature groups will avoid the adoption of a new stem as much as possible in order to limit over-proliferation or will try to maintain the structure of the classification system by adjusting novel stems to be as close to those of similar classes.<sup>9</sup>

### **FACTORS FOR REJECTION: EXISTING NON-PROPRIETARY NAMES AND TRADE MARKS**

Even if a name uses the appropriate stem, there are very practical reasons why a non-proprietary name might not be adopted. Whether one is vying for an INN or only a national name, the number of existing non-proprietary names poses a significant challenge to creating one that is also unique. Added to that, the complexity of ensuring the non-proprietary name denotes the compound's scientific classification *and* is not potentially confused with other non-proprietary names or trade marks, the challenge of securing a non-proprietary name becomes a much higher hurdle. The WHO may accept the INN as written or may suggest alternatives, in the case that the proposed non-proprietary name has a conflict.<sup>3,5</sup> Every compound needs to be uniquely identified.

An additional hurdle is that proposed INNs are published for trademark objection. This is a provision of the WHO that safeguards trade mark owners, but if a trademark owner objects within four months, then the process of INN development starts over. If the manufacturer has not allocated enough time, the INN development process can jeopardise the timely launch of the product and impact sales.<sup>3,5</sup>

### **FACTORS OF CONFLICT BETWEEN THE NON-PROPRIETARY STEM AND THE TRADE MARK**

As already mentioned, the development of the non-proprietary name is a great service to all interested parties: the general public, the

medical professions, and the pharmaceutical industry. Non-proprietary names identify standards, provide consistency in communication, and — as Mr Robert E. Lee, Jr., Trademark Counsel for Eli Lilly said, 'the non-proprietary name services the brand, allowing for brands to have resonance'. The requirements of developing a non-proprietary stem, however, create significant challenges to the development of trade marks.<sup>3</sup>

All INN stems are managed by the WHO. The WHO regulates the use of INN stems through international and local health authorities who ensure that the non-proprietary language is not absorbed into the commercial sector. To that end, health authorities reject trade marks that embed the full stem or obvious portions of it. Given that some stems are as short as two letters, such as *-ac*, which denotes antibacterials, a number of potential trademark options are negated. Any trade mark that embeds those two letters consecutively can be considered in conflict with the stem. Although there are exceptions, for example, Prozac and Zantac, the threat that short stems pose is significant. To circumvent the problem in trade mark development, it is advisable to avoid embedding short, established stems in the same location where they would ordinarily be in an INN.<sup>3</sup> But the difficulty still exists. Mr Lee explains, 'Having to avoid incorporating the INN in light of such short stems, coupled with the increase in the number of stems leaves very little real estate for trademarks... Eventually there may be no room for trademarks'.<sup>3</sup>

While the limitations of the alphabet constrain one's ability to create unique and differentiated names, the length of the name compounds the problem. An optimal length for a non-proprietary name seems to be fixed at around 12 letters, and around 5–8 letters for a trade mark. The USAN, WHO, and commercial preferences for shorter names reduces the available letter configurations. A global market further complicates things by introducing a multiplicity of registries for

both non-proprietary names and trade marks against which all new names must be vetted. The development of both non-proprietary names and trade marks is indisputably a challenge.

## DOS AND DON'TS

The rules for the development of a non-proprietary name are straightforward, though many, and navigating through the myriad of constraints and advisories can be difficult. Following are, however, some general rules of thumb derived from WHO and USAN Guidelines as well as past development experiences for developing a non-proprietary name:

- (1) DO evaluate the compound's newness and uniqueness. Is the structure or mechanism unprecedented? Or, are there existing structures that have already been codified and to which the compound would naturally be associated from a scientific perspective? Whether or not, knowing the details of the compound's science is essential. The following are some areas to investigate about the drug:
  - Chemical Abstract Services (CAS) name and registry number
  - Structural formula
  - Molecular formula
  - Mechanism of action
  - Receptor or other biological targets such as antibodies, etc.
  - Therapeutic indication
  - Scientific papers and studies on how the drug acts and to what it is similar.<sup>5,6</sup>
- (2) DON'T reference a company name. Nomenclature groups view non-proprietary names that reference the manufacturer as promotional, providing the company with an unfair advantage in the public realm particularly when generic competition emerges and must use the non-proprietary name.<sup>5</sup>
- (3) DON'T overtly reference the brand name if it has already been developed,

and especially if it has been published or established. Again, nomenclature groups view such names as promotional.<sup>5</sup> Furthermore, if a brand name is too similar to non-proprietary language, protecting the exclusivity of the brand becomes difficult when the patent expires. After expiry, generic competition can utilise non-proprietary language and appear similar to the brand.

- (4) DON'T attempt to express a brand message. The generic name is intended as public language for scientific and classification purposes. Encoding brand messages will be viewed as promotional, and linking a brand message to non-proprietary language robs one of exclusivity of that message after patent expiry.
- (5) DON'T hint at a mechanism of action or a therapeutic action that is exclusive to its indication. Often a drug is found to have therapeutic benefits for a variety of indications. Specifying a discrete and particular action can obviate the opportunity to communicate how the drug works against the newer indications.<sup>5</sup>
- (6) DO strive to create distinctive names. Whether it is through the stem alone, or the non-proprietary name as a whole, striving for distinctiveness, when appropriate and possible, will help support the perception of the product as unique and different.<sup>3,5</sup> The following are some hints to derive distinctiveness:
  - Let alphabetical order influence the development of the name: try to be first or last on an alphabetised list of your category — start with an A or a Z, it can be a simple way of standing out in a list
  - Explore syllabification and rhythm as a way to increase difference within an established category: among HIV protease inhibitors, most non-proprietary names had four-syllables and a very similar cadence, accenting the second syllable — *darunavir*,

*indinavir*, *lopinavir*, *nelfinavir*, *ritonavir*, *saquinavir*, and *tipranavir*. The 2003 launches of *fosamprenavir* (GSK's Lexiva<sup>®</sup>) and *atazanavir* (BMS's Reyataz<sup>®</sup>), however, changed the landscape with five-syllable names, and accents on the third syllable

- Investigate whether the stem can be placed in a position other than with previous compounds in the category: for example, GABapentin and preGABalin
- Change the tone — if every other name in a category is full of *x*'s and *z*'s, try softening it with different consonants

### THE MARKETING OF BREAKTHROUGH DRUGS VIA THE NON-PROPRIETARY NAME

For pharmaceutical companies who rely on one or two blockbusters to fuel progress, creating and maintaining exclusivity and investing in distinctive branding is critical. So it follows that most marketers take a keen interest in the development of the brand name for their new chemical entities. The non-proprietary name is, however, a little known tool that can promote newness just as profoundly as can a brand name, particularly when the compound exhibits or represents breakthrough science.

Although traditionally the non-proprietary name does not have a role in marketing, it is a logical device to communicate newness because it designates a new product's active ingredient. Breakthrough drugs often have non-proprietary names with new stems that starkly contrast from the non-proprietary names of existing, in-category compounds. This contrast can be leveraged as a platform for communicating the breakthrough. And, because it is sanctioned as available for the public to use without restriction, the non-proprietary name, unlike the trade mark, is terminology that can be used freely within professional and medical educational contexts.

Take for example the gastrointestinal category and the preparations for GERD, or acid reflux. Prior to 1989, the top-selling treatments were those of the H2 Receptor Antagonist class, all sharing the stem, — *tidine*: *cimetidine* (Tagamet<sup>®</sup>), *famotidine* (Pepcid<sup>®</sup>), and *ranitidine* (Zantac<sup>®</sup>). Then in 1989, Astra and Merck launched *omeprazole* (Prilosec<sup>®</sup>), the first of the Proton pump inhibitors and identified with the stem, *-prazole*. The playing field changed dramatically. By 2001, Prilosec had risen to become the second best-selling drug in the US.<sup>7</sup> Leveraging difference through its class designation and non-proprietary name greatly supported Prilosec's differentiation within a category that was saturated with viable and satisfactory options.

As marketers, we seek newness to provide a voice for communication. While non-proprietary names may have a very practical purpose in identifying substances, they can also present an opportunity to support branding goals via name differentiation. In its entirety, the non-proprietary name can differentiate within a therapeutic category through its rhythm and tone, while its stem alone can both align the product to a mechanism or chemistry, and define a standard to which others would be compared and classified. Because a non-proprietary name exists for as long as a compound is available, a well-crafted, distinctive non-proprietary name can benefit a compound well past its patent expiry.

While manufacturers of originator drugs shape the non-proprietary name to support the communication of novelty and innovation, marketers of generic drugs could leverage this distinctiveness to build upon the legacy of the branded originator. If the generic manufacturer happens to be the originator too, then the manufacturer has surely fully maximised its investment.

### CONCLUSION

Of course, breakthrough nomenclature is limited to truly breakthrough science, but every effort should be made to investigate

new language as a means of elevating your product's scientific difference. Just as nothing about the drug development process is left to chance, all elements concerning the marketing of your product should be thoroughly considered. All nomenclature related to a product, no matter how small in scale, contributes to the overall perception of that product. Therefore, approach the development of your non-proprietary name as more than just a requirement. Proceed with due diligence: whether it is how you talk about your product or how you define it through non-proprietary nomenclature, actively seek every opportunity to assert your difference and create distinction.

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