

## ENSURE PATIENT SAFETY WHEN NAMING BIOLOGICAL MEDICATIONS

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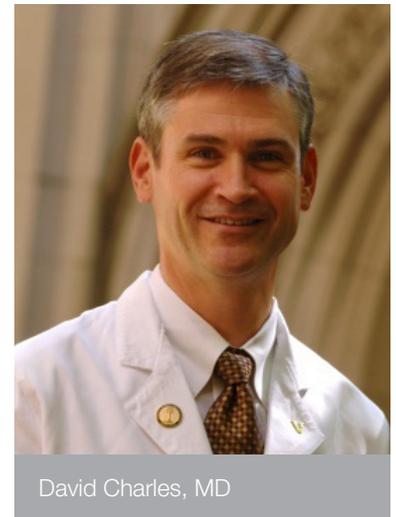
If requiring biological medications to have unique names would help ensure patient safety, wouldn't it be an important convention to implement? The United States Food and Drug Administration (FDA) and several other organizations are currently considering requirements for naming biological medications—those often produced from cells or living organisms. The question is whether biological medications that are similar to one another should have similar non-proprietary names (that is, non-brand names), or whether their names should be identical.

In making this determination, it is critical to recognize that the variations among biological medications can sometimes lead to differences in side effects or immune responses in a given patient. In such cases, physicians must be able to identify exactly which medication caused the reaction so that it can be properly documented and reported, and patients can be switched to a different medication. Only if biological medications have distinct non-proprietary names can the correct medication be identified definitively, quickly, and easily. Thus, to promote patient safety, it is essential that similar biological medications have unique non-proprietary names.

### HOW ARE MEDICATIONS NAMED?

Medications available in the United States typically have several different names. Brand names (also called proprietary names) are proposed by the manufacturers. The proposed names are reviewed by the FDA to make sure that they are different enough from those of other approved medications to avoid confusion.<sup>1</sup> The FDA also ensures that the proposed brand names are not overly promotional—for instance, a brand name cannot imply that one medication is superior to another.

In addition to brand names, medications have non-proprietary names (also called established names) that are determined by the United States Adopted Names Council. Non-proprietary names are meant to indicate certain relationships between medications such as the members of a common class. For instance, some of the biological medications used for cancer, rheumatoid arthritis, and multiple sclerosis belong to a class called monoclonal antibodies. The non-proprietary names of all monoclonal antibodies end in “mab”.<sup>2</sup>



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Generic names are another type of non-proprietary name for medications in which the active ingredient has exactly the same chemical structure as an existing brand-name product. The biochemical analyses conducted to characterize and verify the active ingredients in convention drugs are fairly straightforward. However, the same cannot be said for biologics. Biological medications typically have complex chemical structures that cannot be completely characterized or duplicated. Due to the complexity of biological medications and the difficulty determining their chemical structures, the FDA has determined that, for large and complex biologics, it is not possible to create “generics.” The most that can be said of two biologics is that they are similar, in which case they are described by the term biosimilars.

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## EXAMPLES OF UNIQUE BRAND NAMES AND NON-PROPRIETARY NAMES OF BIOLOGICAL MEDICATIONS IN THE SAME CLASS

Class	Brand Name	Nonproprietary Name
<i>Monoclonal antibodies</i>	Erbitux®	Cetuximab
	Herceptin®	Trastuzumab
	Remicade®	Infliximab
<i>Botulinum toxin type A</i>	Botox®	OnabotulinumtoxinA
	Dysport®	AbobotulinumtoxinA
	Xeomin®	IncobotulinumtoxinA

### WHY IS IT IMPORTANT FOR BIOLOGICS TO HAVE UNIQUE NON-PROPRIETARY NAMES?

Given that biologics have distinct brand names, why is it also important for them to have unique non-proprietary names?

The answer to this question is that physicians and other healthcare professionals often use non-proprietary names rather than brand names to refer to medications. If unexpected side effects do occur, physicians must be able to determine quickly and exactly which medication patients received.

In order to understand why rapid and accurate identification of biologics is so essential, it is important to recognize several points that make these medications unique. First, biologics represent breakthrough therapies for a variety of serious diseases and conditions such as multiple sclerosis, rheumatoid arthritis, and cancer. Before biologics, there were few, if any, treatments for many of these conditions. Today many patients enjoy years of productivity while depending on biologics to slow the progression of their diseases. If the biological medications were to become unavailable, patients could suffer irreversible disease progression or even death. For these reasons, it is critical to ensure that biologics remain safe and available to all patients.

Second, biological medications are extremely complex to manufacture.<sup>3</sup> Whereas conventional drugs are synthesized in a series of chemical reactions in a laboratory, biologics are often produced from cells or living organisms. Biologics are typically large proteins that may be up to 100 to 1000 times larger than conventional drugs and often have intricate three-dimensional structures that are essential to their therapeutic activity. To synthesize and formulate these biochemicals into medications requires a high level of

scientific expertise, and the methods used are proprietary (ie, owned by the manufacturer and not publicly available for duplication by other manufacturers).<sup>4</sup> Even minor differences in the manufacturing processes can affect how biological medications perform in the body of a given patient.<sup>5</sup>

Like any treatment, biologics are sometimes associated with unexpected side effects. In such cases, physicians must be able to trace the exact product that caused the problem so that it can be documented and reported to the relevant organizations. If an individual biosimilar is causing more side effects than predicted, its manufacturer must work to isolate the cause of the problem – a process that could take an extended period of time due to the complex manufacturing processes for biologics. During this time, however, patients can continue to receive treatment from other biosimilar medications that are not causing the side effect.

On the other hand, consider what would happen if the exact medication causing the side effects could not be identified. The prescribing and administration of all similar biological medications in that class would be suspended until the source of the problem was found. In this case, patients would not have access to their medication and their condition could worsen substantially and irreversibly. Furthermore, if similar biologics in the same medication class go by the same name, then physicians and patients may come to associate all of them with the event and thus be reluctant to use them in the future.

This is not merely a hypothetical situation. Several instances have been documented in which the biochemistry of biological medications has been altered by a change in the manufacturing process.<sup>5,6</sup> In one case, a scale-up of the manufacturing process led to the unexpected addition of a chemical group to a biological medication's structure.<sup>6</sup> The

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FDA required the biologic produced in the scaled-up reactor to have a different name than its counterpart.<sup>6</sup> In another instance, a change in product packaging led to unexpected and serious immune responses in some patients.<sup>7</sup> However, because the similar biologics had distinct names, the exact medication could be traced and the source of the reactions identified.

These instances demonstrate the importance of being able to distinguish among biosimilar medications by name. Patient safety is at stake and cannot be relegated for reasons of convenience or economics.

## SHOULD “THERAPEUTICALLY INTERCHANGEABLE” BIOLOGICS HAVE UNIQUE NON-PROPRIETARY NAMES?

Biologics used for a given medical condition may vary in their similarity to one another, although they will not be identical. In some cases, two biologics may be related to one another and used to treat the same condition, but may be used at different doses or have different tendencies to induce antibodies. In other cases, biologics may be considered therapeutically interchangeable if there is enough evidence from clinical comparison studies showing that they are similarly safe and effective when used at the same doses.

However, therapeutic interchangeability does not mean that two biologics are exact generics of one another.

Therapeutically interchangeable biologics from different companies may have different manufacturing steps.<sup>4</sup> Additionally, each company can be expected to introduce changes to its manufacturing process over time, which may result in unexpected changes in the product. Ultimately, each manufacturer is accountable for its own products, regardless of their therapeutic interchangeability status.

This means that the examples mentioned in the previous section also apply to therapeutically interchangeable biologics, namely, if side effects occur, physicians must be able to rapidly and accurately identify which medication a patient received. Requiring all biologics to have unique non-proprietary names would help ensure patient safety in the case of unexpected side effects.

## CONCLUSIONS

Physicians place patient safety at the forefront and believe that it should guide healthcare policies. Biologics are complex

medications that differ substantially from conventional drugs and are regulated differently. In recognition of this, the US FDA has stated that, for large and complex biologics, there can be no generics. It is critical to maintain the distinctions among similar biologics in adopting naming policies. Like the medications themselves, these names can be similar but not identical. Unique names will facilitate the identification of each individual biologic should side effects occur and help ensure patient safety. Instituting a unique naming requirement acknowledges the primacy of patient safety and the scientifically-based variations among similar biologics.

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