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## Beware of legislation that would allow untested copies of biologic drugs

By DAVID CHARLES, M.D.

Congress is considering two bills that could make practicing medicine in the U.S. a much riskier business.

Both bills pertain to state-of-the-art drugs known as biologics. Unlike conventional pharmaceuticals, which are created using simple chemical compounds, biologics are created from living organisms. They have proven to be some of the best treatments available for debilitating illnesses like cancer and multiple sclerosis.

Unfortunately, they are also some of the priciest.

That's why there's a push to expedite the release of imitation, or "follow-on," biologics. The way Congress sees it, since conventional generic drugs cost about 70 percent less than brand-name pharmaceuticals, follow-on biologics could deliver the same benefits as brand-name biologics at a much lower price.

But it's not that simple.

With conventional drugs, the manufacturing process is relatively straightforward and easily standardized. Generics are chemically identical to their brand-name counterparts. There's no need for additional clinical trials to test the generics' safety and efficacy — the fact that the original passed is sufficient.

Producing follow-on biologics, on the other hand, is a far more complex science. Unlike regular pharmaceuticals that typically consist of small molecules, biologics are often much larger and more complex drugs.

Manufacturing a biologic, therefore, is a long and complicated process.

In fact, manufacturing biologics is such a difficult process that no two biological products are exactly the same, and that is why there is technically no such thing as a "generic" biologic. Follow-ons are, at best, rough copies of brand-name biologics — not exact duplicates.

Just look at a recent study in the journal *Movement Disorders* on botulinum toxin type A, one of the more common biologics.

Researchers found that the strength of the toxin varied so greatly from manufacturer to manufacturer that, depending on which drug is used, the proper dosage for treatment of dystonia — a muscular condition affecting the neck — could vary widely

In other words, copies of a brand-name biologic had markedly different therapeutic effects. That's

why follow-on biologics need their own clinical trials before they can be judged safe.

Unfortunately, some in Congress may think otherwise. One of the bills being considered would treat follow-on biologics like traditional generic drugs.

In most cases, a successful clinical trial for a name-brand biologic would vouch for the safety of a follow-on version.

But that's like deciding that a Buick is safe based on the crash-test results of a Rolls-Royce. The two cars share certain features — both have four wheels, a glove compartment, airbags, etc. But they're different enough to warrant separate safety tests.

Similarly, follow-on biologics would share certain fundamental characteristics with brand-name biologics. But they aren't exact copies. And even small variations in their chemical makeup can lead to dramatic differences in their physical effects.

If either one of these bills passes, could countless untested follow-on biologics be rushed to market before anybody knows for sure if they're safe or effective?

As a neurologist, I find this prospect particularly frightening. Finding the correct dosage level for my patients is a difficult process that requires detailed clinical trials. These bills would increase that uncertainty and could needlessly place patients at risk.

If lawmakers determine that it's in the public interest to expedite the approval of follow-on biologics, they need to institute the necessary safeguards. The drugs must undergo separate clinical trials before going to market. Otherwise, there won't be a guarantee they're safe and effective, and physicians won't be able to prescribe them with confidence.

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