intra-manufacturer changes is performed to confirm the established safety and efficacy profile of a marketed biological product after well-defined, incremental process changes have been made by the manufacturer taking into consideration an extensive process and product history linked to clinical experience. A biosimilarity assessment is performed to establish the safety and efficacy profile of a biosimilar product derived from an independently designed manufacturing process where no process history exists and a link to clinical experience has to be established. By default this assessment requires comparative quality, preclinical and clinical data with a reference product. Therefore, it is entirely consistent to argue that a comparable product produced by the same manufacturer should retain its INN, whereas a similar product produced by a different manufacturer should not share an INN with the reference product.

National Drug Codes. The National Drug Code (NDC) cannot possibly serve the function of a distinct name. NDCs are not used in all practice settings and in particular are not commonly used in physician offices or in the inpatient setting. In addition, reporting of adverse events by NDC (a 10-digit numerical code) is highly likely to involve error. Furthermore, use of multiple systems to identify products has value in the effort to protect patient safety. The US Food and Drug Administration has commented publicly on more than one occasion that reliance on NDCs for pharmacovigilance is not a good idea, for the reasons noted above.

In short, the assignment of distinct names to biosimilars and interchangeable products will help assure patient safety and enhance access to medicines at competitive prices. We will continue to work with the regulatory community and other stakeholders to ensure that patients are protected and science prevails.

COMPETING FINANCIAL INTERESTS
The author declares no competing financial interests.

Jim Greenwood

Biotechnology Industry Organization, Washington, DC, USA.
e-mail: jgreenwood@bio.org

1. Anonymous. *Nat. Biotechnol.* **31**, 1055 (2013).

To the Editor:

I read with interest your December editorial[1] concerning international nonproprietary name (INN) rules for the naming of biosimilars and agree with the opinions expressed, especially the last paragraph. I believe the pressure exerted by the Biotechnology Industry Organization (BIO; Washington, DC) and some manufacturers of the original biological therapeutics to promote separate INN naming for biosimilars by the World Health Organization (WHO; Geneva) is part of a strategy to frame biosimilars as different and inferior.

For decades, industry has been producing different, original biological products with different labeling but the same INN: examples include interferon beta 1a and somatotropin. This was apparently never a problem for BIO or manufacturers, so why is it now an issue with biosimilars?

BIO exaggerates the impact of INN naming on the traceability of biosimilar treatment in the case of safety incidents. This is exemplified in the antibody-associated pure red cell aplasia (PRCA) cases occurring after a formulation change of an epoetin product and first reported in 2002. In the cohort of >60 PRCA patients described by Nicole Casadevall, who discovered this side effect, only three received this epoetin only, complicating the linking of the safety issue to the specific product. Relying on INN alone also makes it impossible to identify the relatively common batch-dependent safety issues. Registering the batch given to individual patients is far more logical and is also made relatively easy using the bar codes present on the product packages.

I agree with the editorial that the introduction of biosimilar INN naming implies that originator products should likewise be renamed after major manufacturing changes. In 2011, in this journal, Scheistl *et al.*[2] showed major differences introduced by such changes, exceeding the differences accepted between reference product and biosimilar. None of these changes were mentioned in the product information, and physicians were therefore unaware that they were treating patients with a different product.

There are also some practical problems to solve before the INN system can be applied to biosimilars. It is a passive system, and an INN is only issued by the WHO on request. Transforming this into a mandatory and enforceable system will be virtually impossible. Also, an INN can only be given to a defined chemical structure, whereas biologicals are nearly always mixtures of naturally occurring or process-induced variants. For example, both epoetin alfa and epoetin beta are mixtures of five or six naturally occurring major glycoforms with significant differences in glycan structure. The alfa or beta suffix in the INN designates a defined glycan structure. But the INN of the epoetins has never been attached to a specific glycoform.

The *apartheid* regime for biosimilars advocated by BIO is only part of its policy to defame these products as inferior and to block their market introduction. Developing countries are currently an important target for BIO, where affordable biosimilars are the only means for most patients to be treated with biologics. Therefore, governments in countries like Colombia are introducing legislation carefully designed to allow safe and effective biosimilars while avoiding having regulatory standards impede accessibility. BIO is lobbying fiercely up to the highest political levels for biosimilar guidelines in developing countries that would make the marketing of many highly needed biosimilars impossible. Your editorial is an important signal for governments and regulators and confirms your journal as the voice of reason in a biotech field increasingly dominated by pseudoscience and marketing slogans.

COMPETING FINANCIAL INTERESTS
The author declares no competing financial interests.

Huub Schellekens

Departments of Pharmaceutical Sciences and Innovation Studies, Utrecht University, Utrecht, The Netherlands.
e-mail: h.schellekens@uu.nl

1. Anonymous. *Nat. Biotechnol.* **31**, 1055 (2013).
2. Schiestl, M. *et al. Nat. Biotechnol.* **29**, 310–312 (2011).

***Nature Biotechnology* responds:**

Our editorial simply asked for consistency in the standards to which innovator manufacturers and biosimilar manufacturers are held with respect to international nonproprietary names (INNs). Is it truly scientific to state that comparability assessments are always completely different from similarity assessments and that the kind of intra-manufacturer changes in the processing and production of a brand biologic under a comparability assessment would never result in changes to the product that would warrant a change in INN?