

**AMERICAN COLLEGE OF
RHEUMATOLOGY
POSITION STATEMENT**

SUBJECT: Biosimilars

PRESENTED BY: Committee on Rheumatologic Care

FOR DISTRIBUTION TO: Members of the American College of Rheumatology
Medical Societies
Members of Congress
Health Care Organizations/Third Party Carriers
Managed Care Entities

BACKGROUND:

1 Biological response modifiers or 'biologics' are a class of medications produced by living cells
2 using recombinant DNA technology. They typically fall into three categories: (1) products that
3 are almost identical to natural products the body makes, which are often used as replacement
4 therapy or to augment the body's own response; (2) monoclonal antibodies that bind to soluble or
5 cell surface proteins and block pathways or cells; and (3) engineered proteins that mimic
6 receptors (soluble receptors or receptor antagonists), but are soluble and designed to be stable in
7 humans. Biologics have had an important impact in many areas of medicine, and in particular in
8 rheumatology. However, the high cost of these agents is a growing concern, particularly as more
9 products become available and their use for the treatment of immune-mediated inflammatory
10 diseases continues to expand.

11

12 Biosimilars, also called follow-on biologics, have been viewed as a potential cost-saving
13 alternative to traditional therapies. Currently a product can be considered biosimilar to a
14 reference product if, based on data derived from analytical studies, animal studies, and a clinical
15 study or studies, the product is shown to be 'highly similar' to the reference product,
16 notwithstanding minor differences in clinically inactive components, and if there are no
17 clinically meaningful differences in terms of safety, purity and potency. In addition, a biosimilar
18 product may be deemed 'interchangeable' if it meets certain higher standards. To meet these
19 standards, it must be demonstrated that a product can be expected to produce the same clinical
20 result as the reference product in any given patient, and, if the biologic is administered more than
21 once to an individual, the risk in terms of safety or diminished efficacy of alternating or
22 switching is not greater than the risk of using the reference product without switching. An
23 interchangeable product may be substituted for the reference product by a pharmacist without the
24 intervention of the prescribing health care provider.

25

26 The Biologics Price Competition and Innovation (BPCI) Act of 2009 establishes an abbreviated
27 approval pathway for biologics demonstrated to be biosimilar to, or interchangeable with, an
28 FDA licensed biological product. The objectives of the BPCI Act are conceptually similar to the
29 Drug Price Competition and Patent Term Restoration Act of 1984 (also known as the Hatch-

30 Waxman Act) that established abbreviated pathways for the approval of generic drugs. The FDA
31 is currently (up until December 31,

32
33 2010) soliciting comments on issues and challenges associated with implementing the BPCI Act.
34 A public hearing was held in early November 2010 where over 40 individuals representing
35 pharmaceutical companies, patient advocacy organizations and foundations, physician
36 professional societies, academia, biotech companies, pharmacies, medical student associations,
37 and other corporations expressed a diversity of opinions on how to implement the BPCI Act.
38 Although safety and efficacy are everyone's first priorities, there is tremendous disagreement on
39 what studies need to be done to establish a new product as biosimilar and interchangeable.

40
41 **POSITION:**

42
43 The ACR strongly believes that safe and effective treatments should be available to patients at
44 the lowest possible cost. However, decisions about biosimilarity and interchangeability must be
45 driven by sound science that takes into account several observations and guiding principles,
46 including:

- 47
48 1. The size, complexity, and heterogeneity of biologics (and thus biosimilars) necessitate a greater
49 degree of scrutiny in their analytical evaluation than what is typically required for small molecule
50 generics.
51
- 52 2. Subtle differences in the production of biologics can dramatically affect their functional
53 properties in ways that are not readily predictable. For example, production of the same biologic
54 in different cell lines may result in products with different post-translational modifications with
55 functional consequences.
56
- 57 3. Distinct biologics that target the same molecule are not identical in terms of efficacy and toxicity
58 in clinical use.
59
- 60 4. A biosimilar proven effective for one indication may not necessarily be effective for a second
61 indication for which the reference compound has been shown to be effective.
62
- 63 5. Different biologics may require different degrees of testing to establish safety and efficacy. It
64 may be necessary to consider each biologic separately.
65
- 66 6. Long-term post-marketing registry-based data collection is necessary to monitor for less common
67 but nevertheless important adverse events.
68
- 69 7. Post-marketing surveillance studies are needed in children as well as adults, as toxicities and
70 long-term sequelae may be different. The Best Pharmaceuticals for Children Act (BPCA), which
71 reauthorizes the pediatric studies provision of FDA Modernization and Accountability Act to
72 improve safety and efficacy of pharmaceuticals for children, should apply to biosimilars.
73
- 74 8. The decision to substitute an interchangeable product should not be made without the prescribing
75 health care provider's knowledge.
76
- 77 9. Biosimilars should have distinct names allowing them to be distinguished from their reference
78 products.

79 In light of these considerations, the ACR position is that safety and efficacy of most biosimilars
80 used in patients with rheumatic diseases will need to be established in human subjects in
81 comparison to another established agent in the same class. While cost savings are highly
82 desirable, the approval process for biosimilars (generic biologics) needs to place safety and
83 efficacy, supported by scientifically sound evidence, as the highest priorities.