



Figure 6.4 The role of critical difference in establishing biosimilarity. (From Amgen Inc., Critical quality attributes, <http://www.amgenbiosimilars.com/the-science/critical-quality-attributes/>. With permission.)

and immunogenicity profiles. Note that for stand-alone development, a stand-alone molecule undergoes repeated clinical and nonclinical testing to determine CQAs. Once the CQAs are established, the risk analysis begins—how to assure that during commercial manufacturing, the CQAs shall remain within limits. Since it is not expected that all attributes will be the same, how similar is similar is depicted in Figure 6.4, where variation in CQAs leads to nonsimilarity.

The risk assessments are identified as logical linkages between product development stages and as tools to integrate prior existing product knowledge. The risk assessment process as defined by the ICH for Quality Risk Management (ICH Q9) is used to identify risk elements. Regarding product quality, strict specifications based on the originator’s quality profile are defined for biosimilars, which have to be met accordingly. As the production process of the originator product is undisclosed, no process development and manufacturing knowledge is available for follow-on biologics producers. These differences should be considered to fit risk management to the purposes of biosimilar process development. The risk assessment process as described in ICH Q9 should be reviewed and developed accordingly.

6.3 The risk assessment process

The three-step model initiates risk assessment with the identification of risk by understanding the linkage between the analyzed steps of product development, for example, between CQA and critical process parameter (CPP) selection (Figure 6.5). To visualize the logical linkage and to sort