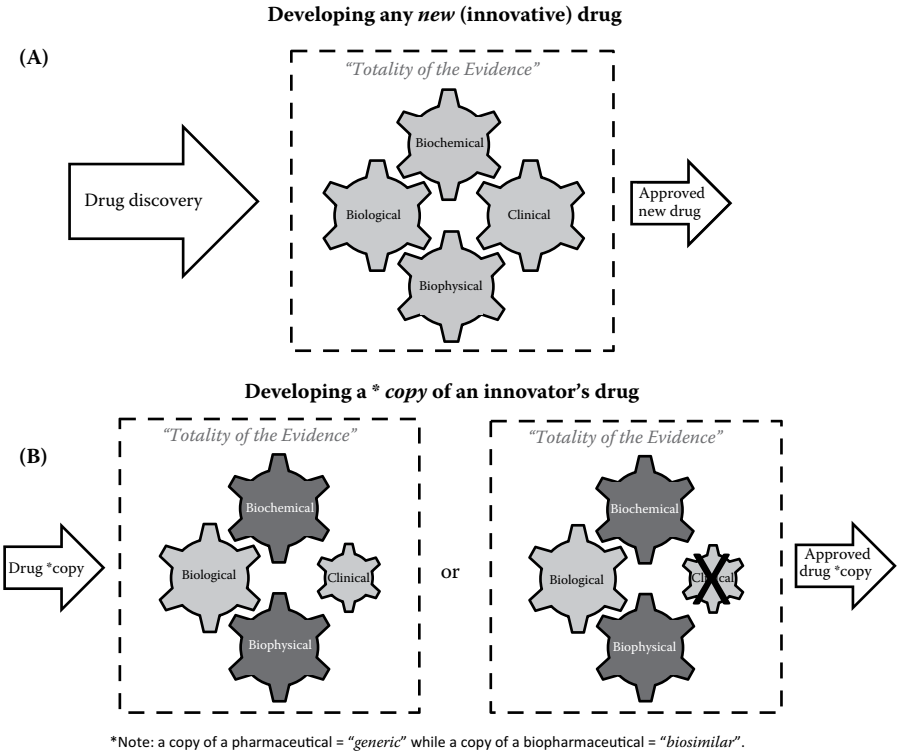

FIGURE 2.1 A simple pictorial view of the key development areas responsible for generating the *Totality of the Evidence* (a phrase, introduced by the FDA that has become associated with the underlying approach for evaluating and approving biosimilars, which, in reality should be applied more universally, as indicated here, to the evaluation and approval of *all* drugs) data package for supporting a drug's regulatory approval: (A) for a new or innovative drug (pharmaceutical or biopharmaceutical) relative to (B) a highly similar or identical copy of an innovator's drug, where the time and cost intensive search of drug discovery is replaced with the less intensive task of demonstrating that an appropriate drug candidate is an adequate copy of an innovative drug resulting in a significant reduction or elimination of clinical data to obtain its regulatory approval. (Reprinted from Houde JD and Berkowitz SA eds., 2014a. Biophysical characterization: an integral part of the "Totality of the Evidence" concept. In: *Biophysical Characterization of Proteins in Developing Biopharmaceuticals*, 385–396. Elsevier, Amsterdam. With permission from Elsevier with minor modifications.)

innovator's pharmaceutical and its generic. In addition, the nature and amount of impurities in the innovator's pharmaceutical and its generic can also be accurately assessed and compared typically using the same mentioned analytical physicochemical tools used to demonstrate structural identity. Once a generic's structural identity to the innovator's drug is established along with a comparable level of purity, bioequivalence, and stability, the generic manufacturer is in a position to take advantage of the long established clinical history of efficacy and safety of the innovator's drug to support the clinical performance of its generic. As a result,