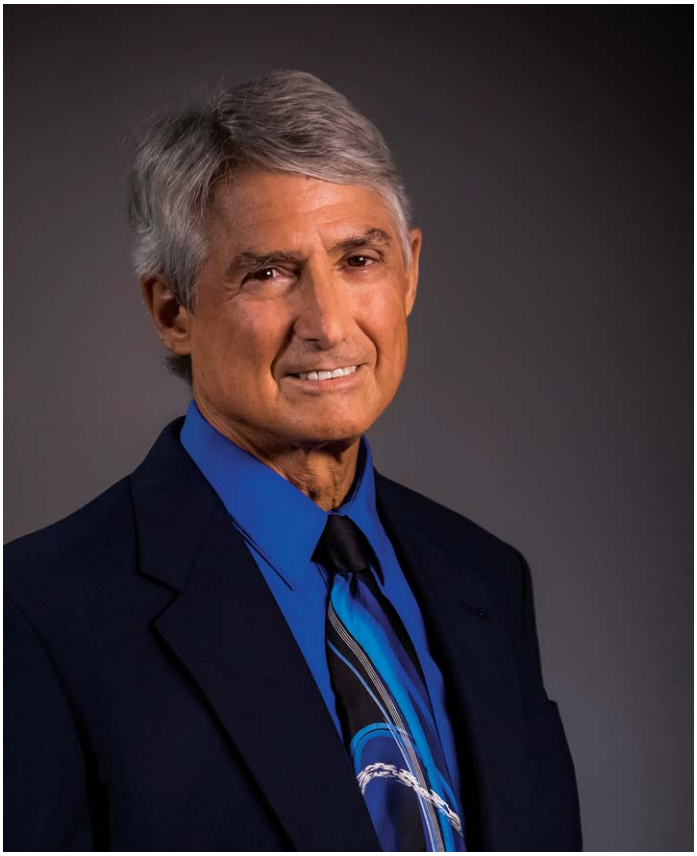
Q&A

Real-World Evidence and Health Technology Assessment: An Interview with Dennis Raisch, PhD



Value & Outcomes Spotlight had an opportunity to talk with Dennis Raisch, PhD, Professor, University New Mexico College of Pharmacy, Albuquerque, NM, USA. Dr. Raisch served as ISPOR Chair of the Risk Benefit Special Interest Group from 2004 to 2012 and as Chairman of the Student Chapter Faculty Advisory Council 2015-7.

Dr. Raisch's interests include research regarding the effectiveness, safety, public policies, and adoption of biosimilars, and the identification of rare, serious adverse events associated with pharmaceuticals, including biologicals.

Value & Outcomes Spotlight: **Why do you think there is substantial variability in the uptake of biosimilars across different countries?**

Dennis Raisch: There are several reasons. First, the FDA was slower in providing regulations for biosimilars compared to Europe. The regulatory pathway was not finalized in the United States until 2015 compared with 2005 by the European Medicines Agency (EMA). The first biosimilar was approved by the EMA in 2006 compared to 2015 in the United States. Second, patent litigation occurs more frequently in the United States and results in marketing delays and added costs. For example, although the first United States biosimilar (filgrastim-sndz) was approved in March 2015 it was not marketed until November 2015. The patent litigation process can be very costly and significantly delay market access. Third, most state boards of pharmacy regulations regarding interchangeability of biosimilars require that the FDA specify that the product is interchangeable. The FDA has not designated any of the approved biosimilar products as interchangeable.[1] Fourth, as with generics, there is resistance from patients regarding use of biosimilars, especially if they have already begun treatment with the reference product. Many state board of pharmacy regulations include requirements for patient acknowledgement that a biosimilar is being used. Unless biosimilars provide significant cost savings for the payer and the patient (regarding their co-pay), the incentives to use biosimilars is insufficient.

What steps should the scientific community be doing to ensure post-approval studies of biosimilars are generating valid evidence?
The most important step will be assessment of effectiveness and safety. Although post-approval studies might be accomplished with large database analyses, it may take several years to acquire sufficient numbers of patients to identify differences. In addition, the details required to accurately specify differences is unlikely to be captured in administrative databases. Studies using patient registries would be ideal to address these concerns. Post-approval randomized, controlled clinical trials (RCTs) could be implemented, but these studies are very costly and unlikely to be large enough or long enough to identify differences in safety. Pragmatic trials with sufficient methods to address bias and confounding will be helpful. Cost effectiveness analyses, systematic reviews, and meta-analyses will be needed. Regarding safety, other types of active pharmacovigilance with specific data collection tools might be feasible in some situations.

What are the biggest challenges in conducting post-approval studies of biosimilars?

Patient registries, RCTs, and active pharmacovigilance studies can be very costly and results may not be available for many years. Furthermore, until uptake of biosimilars increases, it will be difficult to conduct post-approval studies. Specifically, large numbers of patients exposed to biosimilars are needed to make valid comparisons to reference products in post-approval studies. For example, pharmacovigilance research for a safety concern occurring in 1 in 1000 patients would require at least 3000 patients exposed to the biosimilar. Implementing methods to address bias and confounding in observational studies can increase those sample size requirements substantially.

What evidence do stakeholders (physicians, payers, patients) need to accept biosimilars once they are approved, particularly for indications that received approval through extrapolation?

Education is a key requirement to stimulate uptake of biosimilars. Among patients and even prescribers, there is limited awareness or understanding of biosimilars. Given baseline understanding, post-approval research of safety and effectiveness is needed. This applies for all indications, including those approved through extrapolation.

Do you anticipate any difference in uptake of the monoclonal antibodies for the oncology indications than what we have seen with the uptake of anti-TNFs?

The psychological impact of life or death associated with oncologic indications further limit the willingness of patients and providers to use biosimilars.

If you had a magic ball to see into the future, what will the global biosimilar market look like 10 years from now?

Globally, biosimilar utilization will continue to grow and eventually biosimilars will be prescribed in a similar manner as generics and considered equivalent in safety and effectiveness as reference products. That scenario will lead to price reductions of reference products. Another response by pharmaceutical companies will be to continue to develop new biologicals, as well as to improve and modify reference biologicals (ie, biobetters). The uptake of biosimilars in the United States will continue to lag, unless a more efficient and centralized healthcare system is adopted.

REFERENCES

1. https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm580430.htm for more information). Also, see the Purple Book, which lists all approved biosimilar products (https://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/therapeuticbiologicapplications/biosimilars/ucm411418.htm)