PHARMACOVIGILANCE

How adverse events are detected, assessed, and understood throughout a product's life cycle[1]

Overview of safety in **clinical trials** … * VS … **the real-world setting**

Trial participants are selected according to **pre-specified eligibility criteria**[2,3]

In randomized controlled trials (RCTs), incidence of adverse events (AEs) with a product is **compared with a control** (eg, placebo)[4-6]

In clinical trials, all **AEs are reported for the study duration** (including controlled and open-label phases) **regardless of causality**[2,3,5,6-8]

A **larger and more heterogenous patient population** use the approved/marketed product in the real-world setting (eg, patients with more complex comorbidities)[9,10]

Establishing whether a causal relationship exists between real-world AEs and the drug **is challenging because:**

- There may be **unidentified or unaccounted for confounding factors**[10]
- The incidence of real-world AEs includes **background rates of the affected population**[10]

In the post-marketing setting, **the manufacturer must communicate all AEs** that are reported to them to regulatory agencies **regardless of causality**[11]

AEs are **communicated to regulatory agencies** according to specified timelines[11,12]

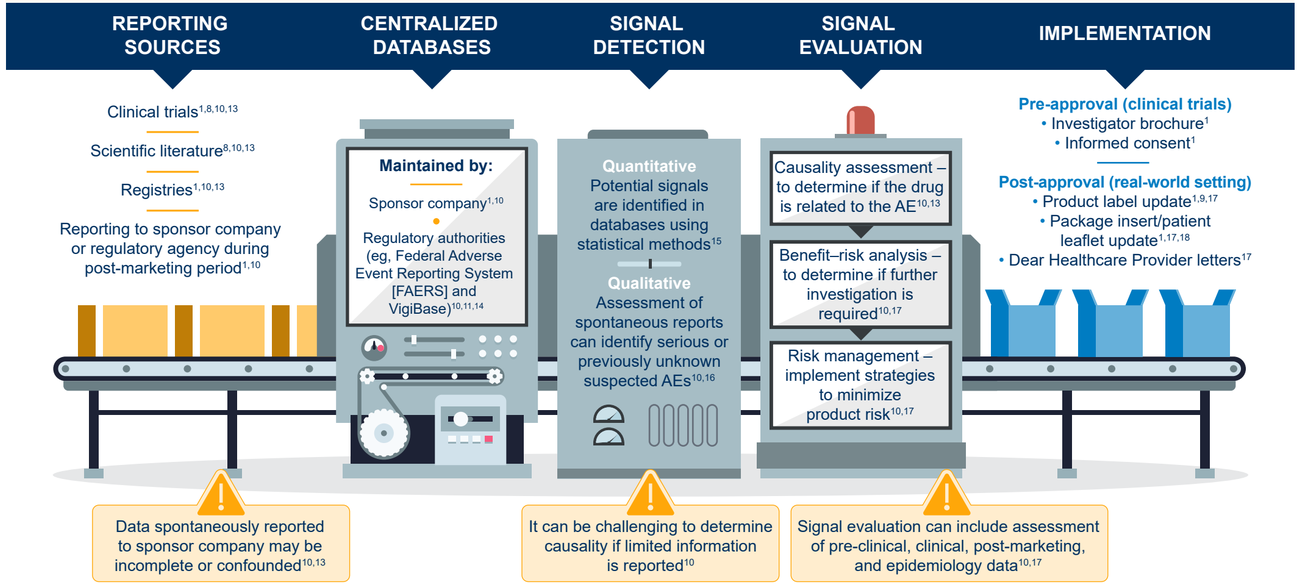
*Refers specifically to manufacturer/company-sponsored clinical trials.[5,7]

AMGEN®

USA-334-83079

See reverse for information on safety signal detection, evaluation, and management ❯

How are **safety signals** detected, evaluated, and managed?



Sponsor companies communicate individual AEs and signals to regulatory agencies via **individual case study reports** and **periodic aggregate safety reports** according to timelines specified by regulatory guidelines[1,9,10,12]

Regulatory authorities have the final decision on the content and language included in the product label and what subsequent action may be required if signals are identified post-approval[8,9,17,19,20]

1. Beninger P. *Clin Ther*. 2018;40:1991-2004. 2. Singh S, Loke YK. *Trials*. 2012;13:138. 3. WHO. Safety of Medicines. A guide to detecting and reporting adverse drug reactions. 2002. 4. Ioannidis JPA, et al. *Ann Intern Med*. 2004;141:781-788. 5. Lineberry N, et al. *BMJ*. 2016;355:i5078. 6. Berlin JA, et al. *Am J Public Health*. 2008;98:1366-1371. 7. FDA. Guidance for Clinical Trial Sponsors. Establishment and Operation of Clinical Trial Data Monitoring Committees. 2006. 8. FDA. Guidance for Industry. Safety Labeling Changes. 2013. 9. Kumar A. *Am J Health-Syst Pharm*. 2017;74:606-612. 10. FDA. Guidance for Industry. Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment. 2005. 11. FDA. Questions and Answers on FDA's Adverse Event Reporting System (FAERS). www.fda.gov/drugs/surveillance/fda-adverse-event-reporting-system-faers. Accessed July 23, 2019. 12. FDA. Guidance for Industry. Providing Submissions in Electronic Format. Postmarketing Safety Reports. 2014. 13. EMA. Guideline on good pharmacovigilance practices (GVP). 2017. 14. WHO. Open Access to the WHO Global Pharmacovigilance Database. www.who.int/medicines/news/glob_pharmvig_database_qa/en/. Accessed July 23, 2019. 15. Koutkias VG, Jaulent MC. *Drug Saf*. 2015;38:219-232. 16. EMA. Guide on the interpretation of spontaneous case reports of suspected adverse reactions to medicines. 2017. 17. Council for International Organizations of Medical Sciences Working Group IV. Benefit-Risk Balance for Marketed Drugs: Evaluating Safety Signals. 1998. 18. FDA. Guidance for Industry. Development of a Shared System REMS. 2018. 19. FDA. Guidance for Industry and Investigators. Safety Reporting Requirements for INDs and BA/BE Studies. 2012. 20. FDA. Guidance. Classifying Significant Postmarketing Drug Safety Issues. 2012.

AMGEN®