The drug approval process is no easy task. From extensive preclinical work to 3 phases of clinical testing and a final approval procedure, the road is long and winding. In fact, on average, the entire process takes between 8 and 12 years. In the United States, drug development is regulated by the US Food and Drug Administration (FDA); the European Medicines Agency (EMA) coordinates the process across many nations. Although the differences between the countries’ regulations are primarily organizational, they share similar objectives, including “promoting and protecting public health, evaluating the safety and efficacy of therapeutic products, working collaboratively with outside experts, reducing the regulatory burden through international harmonization, providing regulatory and health information, and enhancing product development.” In this month’s column, we take a tour of the FDA as an agency and the EMA as a reviewing body to better understand how both promote scientific excellence in the evaluation of medicines.

THE FDA

The FDA is a centralized agency responsible for “protecting the public health by assuring the safety and effectiveness of drugs, biological products, medical devices, the nation’s food supply, cosmetics, and products that emit radiation” in the United States. Although the agency was not known as the FDA until 1930, contemporary regulatory functions began in 1906 with the passage of the Pure Foods and Drugs Act. Effective drug regulation, however, is only half a century old, as the safety and efficacy of drugs have been required only since 1938 and 1962, respectively. The US Food, Drug, and Cosmetic Act passed in 1938 required new drugs to be shown safe before marketing, which mandated FDA regulators to review both preclinical and clinical test results for new drugs. A worldwide drug disaster in 1961 of thalidomide, a new sleeping pill, resulted in the enactment of the 1962 amendments, which strengthened the guidelines for drug safety and obligated manufacturers to certify their drugs’ effectiveness.

Unfortunately, the complete evaluation of a drug’s safety and adverse events cannot be guaranteed in premarketing clinical trials, despite their length and the high number of patients involved.

THE EMA

The EMA is a decentralized agency of the European Union (EU). Created in 1995, it is responsible for the scientific evaluation of applications for authorization to market medicinal products in Europe. The EMA works with a network of more than 4500 European experts who serve as members of the EMA’s 6 scientific committees, including the Committee for Medicinal Products for Human Use (CHMP). It comprises over 40 national authorities in the 27 EU Member States and the Economic Area-European Free Trade Association (EEA-EFTA) countries of Iceland, Liechtenstein, and Norway. In the EU, medicines can be authorized by the centralized authorization procedure or national authorization procedures.

A centralized authorization procedure is mandatory for medicines for the treatment of HIV/AIDS, cancer, diabetes, neurodegenerative diseases, autoimmune dysfunctions, and viral diseases; medicinal products developed by biotechnologic processes (eg, ranibizumab [Lucentis, Genentech] and aflibercept [Eylea, Regeneron]); advanced-therapy medicines; and desig-
Each EU Member State has its own procedures “for the authorization of medicines that fall outside the scope of the centralized procedure.”

Companies with medicines that do not fall within these categories have the option of submitting an application for centralized marketing authorization to the EMA. Once the EMA has made an assessment regarding whether a medicine should be marketed or not, the opinion is transmitted to the European Commission, which holds the final approval. The centralized authorization, once granted, is valid in all EU and EEA-EFTA counties.

Apart from the centralized authorization procedure, each EU Member State has its own procedures “for the authorization of medicines that fall outside the scope of the centralized procedure.” A sponsor can also seek approval of several EU countries simultaneously via 2 alternative routes: the decentralized procedure and the mutual recognition procedure. For products that fall outside the restrictions of a centralized procedure, a decentralized procedure allows simultaneous authorization in more than 1 EU country for products that have not been authorized in any EU country. With the mutual recognition procedure, a product is authorized by 1 country in the EU via its respective national guidelines; subsequently, marketing authorizations can be given to other EU countries who agree to recognize the decision of the first country.

HOW THE DIFFERENCES TRANSLATE

Because the FDA is a single approval and enforcement agency, it has some advantages over the EMA, particularly in a crisis, because it does not have to coordinate among many states or countries. The EMA is a secretariat for a network of experts, but, unlike the FDA, it does not have the final word on drug approval (the European Commission does). Additionally, while the EMA coordinates marketing authorization for the EU nations, the Member States are responsible for enforcement, maintaining licensing, and controlling sales and promotional activities of drugs. The FDA and the EMA also have different requirements for the approval and use of medical devices. The FDA requires valid scientific evidence that devices are both safe and effective. By contrast, the European CE mark requires only proof of safety and that the device performs in a manner consistent with the manufacturer’s intended use.

Despite their differences, both the FDA and the EMA are geared toward a similar goal: the evaluation of the quality, safety and efficacy of medicinal products. One particularly important similarity is partnership with the International Conference on Harmonization (ICH) and adherence to document guidelines. Further, the signing of confidentiality arrangements in September 2003 increased the level of cooperation between the EMA and the FDA. The exchange of letters took place as part of the regular cycle of EU-FDA bilateral meetings that have taken place since 1989. The agreement allows the EMA, FDA, and the European Commission to exchange information as part of their regulatory processes, both pre- and postapproval.

Aron Shapiro is Vice President of Retina at Ora, Inc., in Andover, MA.
Ashley Lafond is a medical writer at Ora, Inc.