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New Comments from FDA Commissioner Scott Gottlieb, M.D., Regarding the Expanded Access Program and the Right to Try Act

In an earlier article authored by Ropes & Gray attorneys, we summarized the implications of the "Trickett Wendler, Frank Mongiello, Jordan McClinn, and Matthew Bellina Right to Try Act of 2017" ("RTT"). President Trump signed RTT into law in May 2018 to provide patients who are not eligible for enrollment in a clinical trial with a pathway to obtain investigational drugs or biologics for therapeutic use. There is an existing expanded access ("EA") pathway, however, referred to colloquially as "compassionate use," that also provides access to investigational products for therapeutic use. Generally, under both pathways, the eligibility criteria are similar: the patient must (1) have a life-threatening condition for which no other treatment is available, (2) have exhausted available treatment options, and (3) be unable to participate in a clinical trial. Both pathways also require manufacturer approval and informed consent of the patient. However, access though the RTT pathway removes administration of the investigational product from institutional review board ("IRB") and Food and Drug Administration ("FDA") oversight, among other changes.

Questions have been raised by both pharmaceutical manufacturers and health care providers regarding the interplay between EA and RTT. The regulated community received some clarity on this topic on November 8 with the comments of FDA Commissioner Scott Gottlieb, M.D. Commissioner Gottlieb's comments reveal that the FDA continues to view EA as a valuable pathway for providing investigational products outside of a clinical trial to patients with serious or life-threatening diseases who lack other treatment options. Moreover, the Commissioner's comments suggest that the FDA seeks to demonstrate that it has been and will continue to be responsive to concerns regarding access to investigational drugs through the EA pathway.

As summarized at a high level by Commissioner Gottlieb, the FDA has recently made several changes to the EA program to facilitate access to investigational therapies through the EA pathway:

- First, the FDA published a new form that streamlined the documentation physicians must submit to FDA in support of EA requests for investigational drugs or biologics for treatment of individual patients. FDA estimates that this form takes only approximately 45 minutes to complete.

- Second, the FDA updated its EA guidance to state that a physician requesting an individual patient expanded access IND may request waiver by FDA of the full IRB review requirement and instead obtain concurrence by the IRB chairperson or another designated IRB member before treatment use begins. *See* 21 C.F.R. § 56.105 (permitting FDA to waive the requirement for full IRB review upon request from the sponsor or sponsor-investigator). This simplified IRB review process is similar to the "expedited" review procedure that IRBs can follow for certain minimal risk research. *See* 21 C.F.R. § 56.110 (setting forth requirements for expedited IRB review).

- Third, the FDA clarified in the revised EA guidance the criteria by which it evaluates safety data generated from use of an investigational drug or biologic through the EA pathway, intending to recognize and address companies' concerns that EA-related adverse event data could complicate or impede the drug review and approval process. The revised guidance explains, among other things, that FDA reviewers recognize that EA treatment generally occurs outside a controlled clinical trial setting and that patients receiving a drug through EA may suffer from more advanced disease than those in a clinical trial, may be receiving other therapies, and may suffer from one or more comorbidities, all of which make it difficult to link an EA treatment to a particular adverse event. FDA also states that it is very rare for the agency to place an IND on clinical hold due to adverse events observed in EA treatment.

- Fourth, the FDA commissioned an independent assessment of the EA program to incorporate comments of various stakeholders on the program, such as patients, advocates, health care providers, and health systems. This assessment found positive impressions of the EA program overall, with discussion of some room for improvement around administrative burden, program navigation, and multi-stakeholder coordination. The FDA has sought to implement these comments through making its website more user-friendly and investing in support for patient/physician program navigation. The FDA also recently proposed reorganizing the Office of the Commissioner to include an agency-wide Patient Affairs Staff and Health Care Provider Affairs Program that would serve as a resource for patients and physicians initiating the EA process.

In his remarks, Commissioner Gottlieb also recognized the existence of the RTT pathway. He noted that the FDA has established a working group to consider steps necessary for implementation and launched a webpage designed to explain the RTT program to patients.

Despite the development of RTT, many pharmaceutical manufacturers may elect to continue to use EA as the preferred pathway through which to provide therapeutic access to investigational products. As Commissioner Gottlieb noted, the FDA has authorized approximately 99% of EA requests, and typically does so within a few days of receipt of non-emergency requests, and immediately for emergency requests. When patients are denied access, typical causes include incomplete applications, lack of demonstrated efficacy of the product, unsafe dosing, or availability of alternative therapies. Pharmaceutical manufacturers may prefer the EA pathway because it almost always facilitates prompt access when appropriate, and contains safeguards of IRB and FDA review and approval to prevent access when it would not be appropriate. Ropes & Gray will continue to monitor developments in relevant rules, guidance, and practices as manufacturers, providers, and patients gain additional experience with RTT, and as we continue our close monitoring of the broader topic of access to investigational medical products.