long, trial design may include one or more surrogate endpoints. When included in trial design, surrogate endpoints can reduce the cost and duration of the trial. According to Fleming and DeMets (4) a surrogate endpoint is a laboratory measurement or a clinical sign used as a substitute for a clinically meaningful endpoint. The surrogate endpoint measures how a patient functions, survives, or feels. The surrogate endpoint is supposed to operate as follows. Changes induced by a therapy on the surrogate endpoint reflect changes in the clinically meaningful endpoint.

Examples of surrogate endpoints include tumor size and number, or time to detection of tumor metastasis in clinical trials in oncology, LDL-cholesterol in clinical trials with drugs for atherosclerosis, and reduction in brain lesions in clinical trials on multiple sclerosis. In the context of clinical trials on infections, Smith et al. (5) expressly categorized endpoints as clinical endpoints (relates to signs and symptoms of the infection) and as bacteriological endpoints (measures the titer of the infecting agent).

The proper place of surrogate endpoints in trial design has been reviewed by Dhani et al. (6) Gil and Sargent (7) Pazdur (8) McKee et al. (9) Allegra et al. (10) Hoos et al. (11) Soria et al. (12) Lamborn et al. (13) and Armstrong and Febbo (14).

While surrogate endpoints may be included in the list of endpoints for any clinical trial, surrogate endpoints are of increased importance for the FDA's accelerated drug approval program. According to one of the FDA's Guidance for Industry documents, surrogate endpoints may be a basis for FDA approval for drugs used to treat serious or life-threatening diseases, and "[i]n this setting, the FDA may grant approval based on an effect on a surrogate endpoint that is *reasonably likely* to predict clinical benefit" (15).

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