Setting Eligibility Criteria

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In every clinical trial protocol, regardless of the disease being studied, a section on eligibility criteria is required. Although the criteria will differ from study to study, these rules set the stage for the population that the study will examine, as they include characteristics that must be shared by all study participants. Eligibility criteria include both inclusion and exclusion criteria and may be comprised of age, sex, medical history, current health status, severity of the disease being studies, and concomitant medications. First and foremost, eligibility criteria help to keep study volunteers as safe as possible. They also work to make the study more meaningful by selecting subjects most representative of the study population with the disease to better understand a potential new treatment. A well-thought-out set of inclusion and exclusion criteria will set the stage for study approval by regulatory agencies and appropriate subject selection.

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INCLUSION AND EXCLUSION CRITERIA

Eligibility criteria are far from randomly chosen guidelines, as they will affect who participates in the study, the way the study is conducted, and, consequently, the results. Inclusion criteria are rules about the characteristics that a person must possess in order to participate in a study. Personal characteristics such as age and sex are typically found among inclusion criteria, as well as disease characteristics such as the specific symptoms a person is experiencing. The CATT study, for example, included subjects who were at least 50 years old, had a total area of fibrosis of less than 50% of the total lesion area, had a visual acuity between 20/25 and 20/320, and had active subfoveal choroidal neovascularization (CNV). Viable inclusion criteria help to select participants who are similar in characteristics or who have a similar disease course in order to monitor their reaction to a specific treatment in a measureable way. Meeting all of the inclusion criteria is 1 step in the qualification process for enrollment; however, subjects must also successfully not meet any of the exclusion criteria as well. Should any of the exclusion criteria apply to a participant, he or she would be excluded from participating in the study. Exclusion criteria target specific characteristics such as too severe disease, complications of disease, other medical conditions, and previous or concomitant treatment. Using the CATT study again as an example, exclusionary criteria included previous treatment for CNV in the study eye, fibrosis involving the center of the fovea in the study eye, concurrent treatment with an investigational drug or device, and concurrent use of systemic anti-VEGF agents. By identifying specific characteristics that may put the participant at risk, limit potential efficacy of the study medication, adversely affect the person's condition in a way that makes participation dangerous, or make the individual less likely to successfully complete the study, the study sponsor can enroll the most ideal subjects.

CRITERIA PRACTICALITY

When establishing inclusion and exclusion criteria for a new study, history is often the best indicator of criteria practicality. Once the disease to be studied has been defined, consider looking at prior published studies with similar participants. What were the main inclusion and exclusion criteria? What were the demographics of the population? Is the information applicable to the current study? Enrollment criteria previously used in large, randomized, double-masked clinical trials are often a good starting place for considering new study designs. Additionally, to ensure that a population is homogeneous among treatment groups, it may be necessary to stratify randomization, particularly in smaller studies in which equal homogeneity between the groups is less likely. Evenly distributing the disease characteristics between treatment groups will provide 2 similar popula-

tions to assess treatment efficacy. When assessing endpoints, such as visual acuity, stratifying patient populations will also allow study groups to have similar baseline characteristics.

DESIGN CONSIDERATIONS

Each inclusion and exclusion requirement will ultimately affect enrollment, so it is important to mindfully set the criteria. Defining criteria is a delicate balance between *too much* and *too little*. Care should be taken to avoid requiring difficult-to-assess inclusion criteria or to have many frequently occurring exclusion criteria. Studies with less stringent enrollment requirements may be easier to enroll but may result in a more heterogeneous patient population and leave the study open to confounding factors. Conversely, restrictive enrollment requirements may benefit a trial by making endpoints easier to reach but may make enrollment more difficult. Inclusion criteria should be as specific as needed to isolate the disease being researched without unnecessarily restricting the study population. Another consideration is that the end goal in successful drug development programs is a US Food and Drug Administration (FDA)-approved indication. Small patient populations based on restrictive inclusion and exclusion criteria may lead to restrictive labeling.

CONCLUSION

Choosing inclusion and exclusion criteria is an intricate process that will affect recruitment, enrollment, and, ultimately, the safety and efficacy of a product. Considering previous relevant clinical trials is an efficient way to identify a baseline set of criteria for a novel product. Additionally, weighing the pros and cons of more restrictive vs less stringent eligibility criteria will also play a role in the rate of subject enrollment and potential for FDA approval. ■

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