A new push to show how many women, minorities, seniors and children participate in clinical trials aims to combat a historical bias that critics say has led to medicines that work well for white men but not necessarily for everyone else.

The FDA launched the effort in late 2014 via online “Drug Trial Snapshots” that provided some of the demographics behind the research trials of six newly approved drugs. They immediately revealed glaring racial and gender disparities. With a treatment for Crohn’s disease, nearly 90 percent of study subjects were white. For a toe fungus medicine, men comprised more than three-quarters of those tested.

Starting this year, the agency has pledged to publish such data for every new drug within 30 days of its approval. It’s also adding information. The next three snapshots, which are set to come out next week, will include details on trial participants’ ages.

Officials say they are optimistic that such transparency will spark conversation about the need for far greater diversity in clinical trials to help researchers better understand how drugs affect different groups. “Let’s have a discussion about why does it matter and when does it matter,” said John Whyte, director of professional affairs and stakeholder engagement at the FDA’s Center for Drug Evaluation and Research.

Yet the reaction from advocacy groups and policy experts has been mixed. Some believe the website has the potential to goad industry into broader recruiting. Others consider the snapshots as more of a nudge than real pressure points. They say the FDA should require pharmaceutical companies to include a broader spectrum of participants in research — as NIH has for more than 20 years.

“We think the only way to get companies to step up to the plate and really do a good job of recruiting is to say, ‘We’re just not going to approve your product for people in whom it wasn’t adequately tested,’” said Diana Zuckerman, president of the National Center for Health Research.
Advocates began working on this issue long ago following a 1977 FDA decision to bar women of childbearing age from most early phase clinical trials. Although research subsequently revealed that the decision harmed rather than benefited women’s health, not until 1993 were the guidelines rescinded and replaced with language encouraging the inclusion of demographic subgroups.

Ambien is a drug that groups cite as an example of why still more change is necessary.

Two decades after the sedative first went on the market, the FDA in 2013 halved the recommended dosage for women to account for how much slower their bodies metabolize it. That would have been known from the start had Ambien been tested on enough women before approval, advocates say. Instead, it took hundreds of complaints, with women reporting drowsiness the morning after taking the drug and even some cases of car accidents.

Whyte calls the new snapshots a tool that patients and doctors can use in deciding whether a certain drug is right for the individual. But they’re just a first step in a comprehensive plan to address issues around disparities, as the agency was ordered to do by the FDA Safety and Innovation Act of 2012.

The Society for Women’s Health Research, American Heart Association and several additional groups want it to be a bigger step. They’re pressing for demographic data to be released for past trials, for medical devices and, since FDA currently is only providing phase III detail, for earlier stages of trials. They think the data should be searchable by multiple subgroups so that an African-American woman, for instance, could find out exactly how many of her peers participated.

“This is pressure for industry to realize that they really need to clamp down and make sure that they have subgroup populations included to the extent that the results can be clinically relevant,” said Phyllis Greenberger, SWHR’s president, who acknowledges that the pharmaceutical industry has made strides in incorporating historically underrepresented groups. But it’s not enough progress, she believes. “This, hopefully, will change the way research is done.”

PhRMA has its own issues with the snapshots, saying the omission of information about drugs’ overall safety and effectiveness may mislead patients about whether certain drugs are right for them. The trade group also says that current race and ethnicity categories don’t adequately reflect the diversity of participants.
“There is still a great deal to learn about the biological, anatomical, and physiological mechanisms that underlie disease,” PhRMA wrote in comments submitted to the agency. It recommended supplementing current data with information about disease prevalence in different subgroups.

As the FDA’s effort moves forward, some are also concerned that it could be undermined by Congress’ 21st Century Cures initiative. To get new treatments to patients faster, the initiative proposes speeding up the drug approval process, in part, by reducing the size of clinical trials.

Zuckerman and Susan Wood, former director of the FDA’s Office of Women’s Health, say that smaller studies will not allow for premarket understanding of how differently a drug may affect people based on gender, age, race or ethnicity.

"We’re going to lose the ability to have good information that would populate the snapshots,” Wood said.

Both women have raised these concerns with the House Energy and Commerce Committee, including members like Reps. Lois Capps and Diana DeGette, who they say have previously championed clinical trial diversity. At the same time, they acknowledge subgroup analysis may not be relevant to every trial for every drug — prompting a new set of questions about when diversity is important, if not essential.

In the first snapshots released last year, such analysis made more sense for a drug prescribed to lower the risk of heart attack, stroke or cardiovascular death than for that toe fungal medicine. And with Zontivity, the FDA was able to determine that women have a higher risk than men of internal bleeding. But it couldn’t draw conclusions about differences by race because too few minority patients were part of the clinical testing. More than 87 percent of the 26,449 patients studied were white.

This kind of information has not been readily accessible to the average consumer or provider in the past. Its availability now puts everyone on the same page.

“Collecting and analyzing information in clinical trials about sex, age, and race/ethnicity, makes it possible for individuals or groups considering a treatment option to look at the information and ask, 'Was there anyone like me in the clinical studies? And if so, how did they do?’” noted Barbara Buch, associate director for medicine in FDA’s Center for Biologics Evaluation and Research, in a blog post Thursday.
The Society for Women’s Health Research says that it’s already in discussions with the pharmaceutical industry about the numbers and representation required for statistically meaningful analyses, as well as when such analyses are appropriate. It’s also brainstorming new approaches to recruiting members of target subgroups, such as by social media and mobile device applications.

“We realize that it’s complicated, and it’s probably more costly and time consuming, so we’re not trying to make life difficult for industry,” Greenberger noted. “We want to get it right.”

Whyte said the FDA is open to expanding the snapshots for drugs and medical devices already on the market, but its priority is to release data for upcoming approvals. And according to Buch’s blog post, officials are working with providers, the industry and NIH to ensure that future trials are designed and analyzed with greater demographic inclusion in mind.