In this presentation, I discuss four core challenges to promoting conceptual change and epistemic growth in middle-school science classes. I draw on my research with the PRACCIS (Promoting Reasoning and Conceptual Change in Science) project with Ravit Duncan and colleagues; this project aims to promote students’ reasoning ability and conceptual understanding through model-based inquiry, with argumentation featured as the central discourse. Data come from two implementations of PRACCIS in a total of 44 middle-school classes (with 12 and 13 year olds) taught by 9 teachers. The first challenge is the problem of underdetermination. Our research suggests that, in the practical realities of science classes, model choice is underdetermined by evidence, so that evidence-based arguments cannot be decisive. A second challenge is establishing social norms for reasoned argumentation as the core discourse. Third is the problem that students must succeed in simultaneously changing both epistemic practices and content understanding. Finally, teachers often have difficulty trusting students to take the lead in argumentation. I present data bearing on each of these challenges, and suggest ways in which effective design of inquiry environments can successfully address them. One of the design features that we have found helpful is the use of public epistemic criteria generated and refined by students.