While continuous manufacturing (CM) offers significant advantages over batch, fed-batch, and batch perfusion cultures, it is typically more difficult to screen conditions or troubleshoot issues because of the added complexity to the bioreactor system and the long time duration required to receive representative results. For certain screening factors such as medium, the use of spin tubes (50 mL shaken conical-shape vessels) in a simulated CM (sCM) format can be used to approximate the conditions experienced in an instrumented bioreactor. We will discuss how sCM spin tube performance data was used to troubleshoot bioreactor performance while evaluating five cell lines using multiple medium. Specifically we will show how sCM spin tubes can successfully screen medium performance for parameters such as growth, viability, and productivity. The resultant output from the sCM study was then used to perform a confirmation bioreactor run, with significant process improvement that was in line with expected performance. In summary, we show how sCM spin tubes can be used as an effective tool to screen specific inputs such as media for improved bioreactor performance.