CFD codes. In fact, the sublimation rate can be easily correlated to the operating conditions (shelf temperature and chamber pressure) and to the vial and product characteristics by means of a simple mass balance equation, coupled with an equation stating that the heat flow from the shelf to the product is used to sublimate the ice. This simple model (for the vial) results in the prediction of the sublimation flux value in each point of the computational domain of the CFD simulation (at the chamber scale) and in each instant of time of the drying process, depending on the local vapor pressure, shelf temperature, and thickness of frozen layer. Results obtained with this approach are described below whereas results obtained by using an off-line approach, more suitable for process transfer and scale-up, are presented in the next section.

In Figure 4 (upper line), an example of the typical pieces of information obtained from the dual-scale simulation is shown; in particular, the contour plots for the absolute pressure (Fig. 4A), the interface temperature (Fig. 4B), and the resulting sublimation rate (Fig. 4C) are reported, quantifying the effect of pressure gradients on vials history. As it is possible to see, a difference of about 2 to 3 Pa in the local water vapor pressure results in a variation of about 1 to 2 K in the equilibrium interface temperature, resulting in turn in a variation of 3% to 4% in the sublimation rate. This shows how the CFD two-scale model can be used to design the freeze-dryer. By fixing the maximum allowed sublimation rate difference, it is possible to calculate the maximum pressure difference across a single shelf or in different shelves.

Exploiting even further the two-scale model, it is possible to calculate the maximum tolerated gradients in the heating fluid circulating inside the shelf that result in a given variation of sublimation rate. As an example, in Figure 4 (lower line) the profiles across a shelf of the industrial-scale apparatus for the resulting sublimation rate with a constant heating fluid temperature (Fig. 4C) and with a constant gradient of the heating fluid temperature (Fig. 4D) are reported.

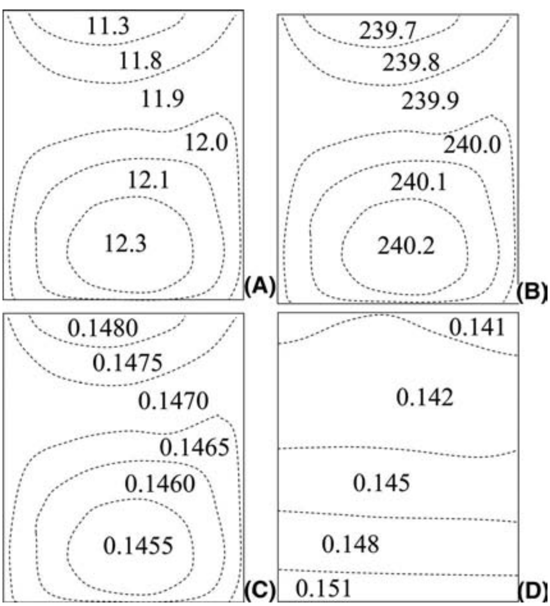

FIGURE 4 Contour plots on the 12th shelf of a LyoMega^{TM} 400 (by Telstar) of absolute pressure, Pa (**A**), interface temperature, K (**B**) and sublimating flux, kg/m^2 h, in the case of heating fluid with constant temperature (**C**) and undergoing a linear variation of 2 K from one end to another (**D**). By permission of Telstar, Terrassa, Spain.