White Paper: The Scale-Up of Continuous-Flow Thermal Processes Using MTI BioScience and MicroThermics® R&D Systems

Subtle yet essential details of commercial processes, such as sterilization, viral inactivation, & DNA inactivation, differ across the industry. These differences dramatically impact the quality and effectiveness of the products being processed. Therefore, the R&D system's impact must closely match the commercial process for accurate research and efficient process development. In addition, detailed analysis of specific client process data may also significantly help optimize the accuracy of the scale-up of the entire thermal process exposure.

MTI BioScience's® R&D systems easily scale up to a wide range of commercial processes. Our equipment's design features and high degree of flexibility make this possible. As a result, many clients get great results "right out of the box ."

However, many clients want more support, so they take advantage of our technical support scale-up service. We can provide a detailed analysis of the client's targeted commercial process. With this, we also provide the configuration and operating conditions for accurate scale-up from the MTI BioScience ® R&D system in their laboratory to their commercial process.

SCALING UP:
First, we must identify the target commercial process for scale-up. We gather the system's design details, configuration, and operating conditions. Then we tabulate the process's heating, holding, and cooling steps. This is shown in Table 1.

Table 1. Client Raw Process Step Duration and Temperatures

Step Number	Purpose	Step Duration	Temperature ˚F	Temperature ˚C
Step 1	Transit	10.00	70.0	21.1
Step 2	Transit	1.00	70.0	21.1
Step 3	Heater 1	25.00	170.0	76.7
Step 4	Transit	3.00	219.9	104.4
Step 5	Heater 2	25.00	289.0	142.8
Step 6	Transit	1.00	289.0	142.8
Step 7	Hold Tube	12.00	288.5	142.5
Step 8	Transit	3.00	288.4	142.4
Step 9	Cooler 1	20.00	188.0	86.7
Step 10	Transit	3.00	187.9	86.6
Step 11	Cooler 2	30.00	70.0	21.1

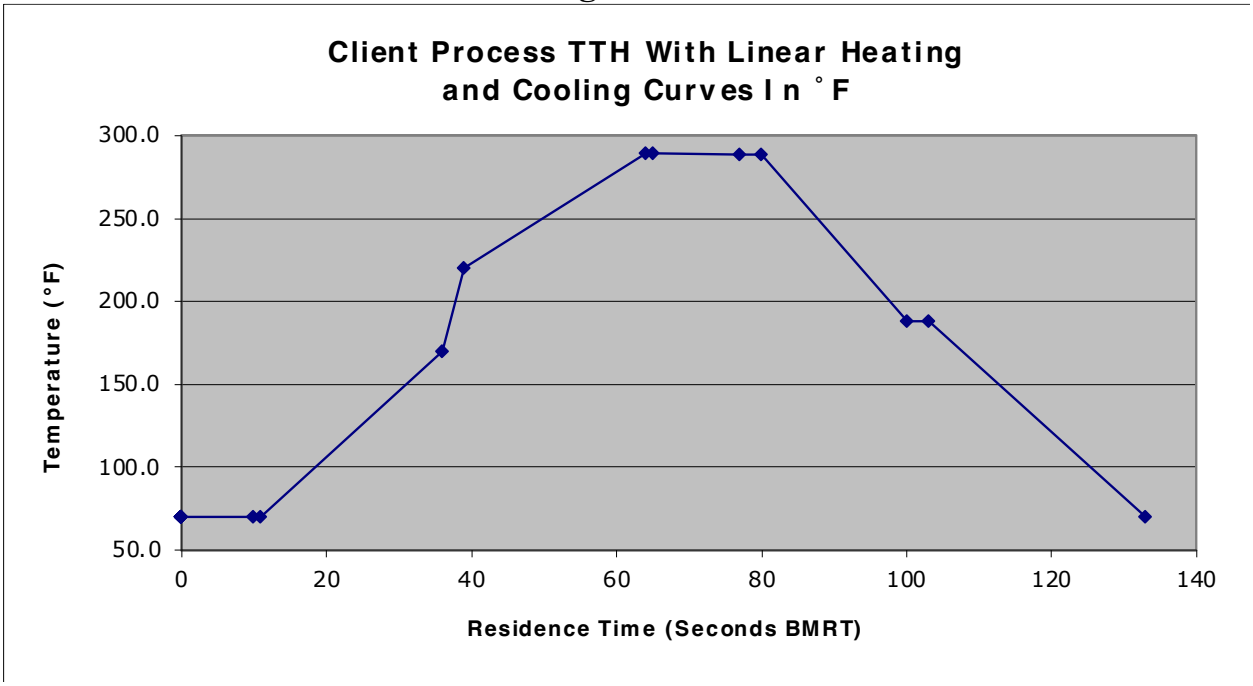
Next, we construct the time-temperature data for the commercial process using this data. This is shown in Table 2.

Table 2. Client Process Time-Temperature History

Step Number	Purpose	Residence Time	Temperature ˚F	Temperature ˚C
Step 1	Transit	10.0	70.0	21.1
Step 2	Transit	11.0	70.0	21.1
Step 3	Heater 1	36.0	170.0	76.7
Step 4	Transit	39.0	219.9	104.4
Step 5	Heater 2	64.0	289.0	142.8
Step 6	Transit	65.0	289.0	142.8
Step 7	Hold Tube	77.0	288.5	142.5
Step 8	Transit	80.0	288.4	142.4
Step 9	Cooler 1	100.0	188.0	86.7
Step 10	Transit	103.0	187.9	86.6
Step 11	Cooler 2	133.0	70.0	21.1

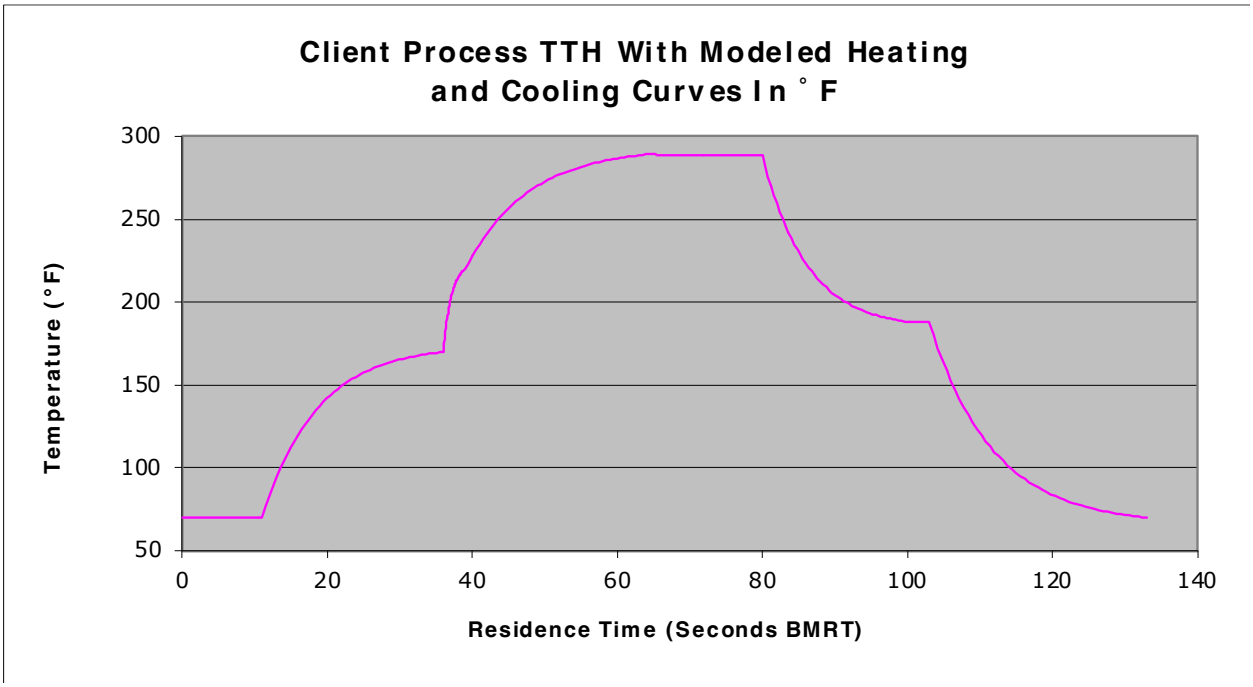
These data are graphed and produce a “linear” Time-Temperature History (TTH) for their process. The data are from only the temperature measurement points of the process and not within the heat exchangers. This limited data produces a TTH showing linear heat steps, as shown in Figure 1.0 below.

Figure 1.0



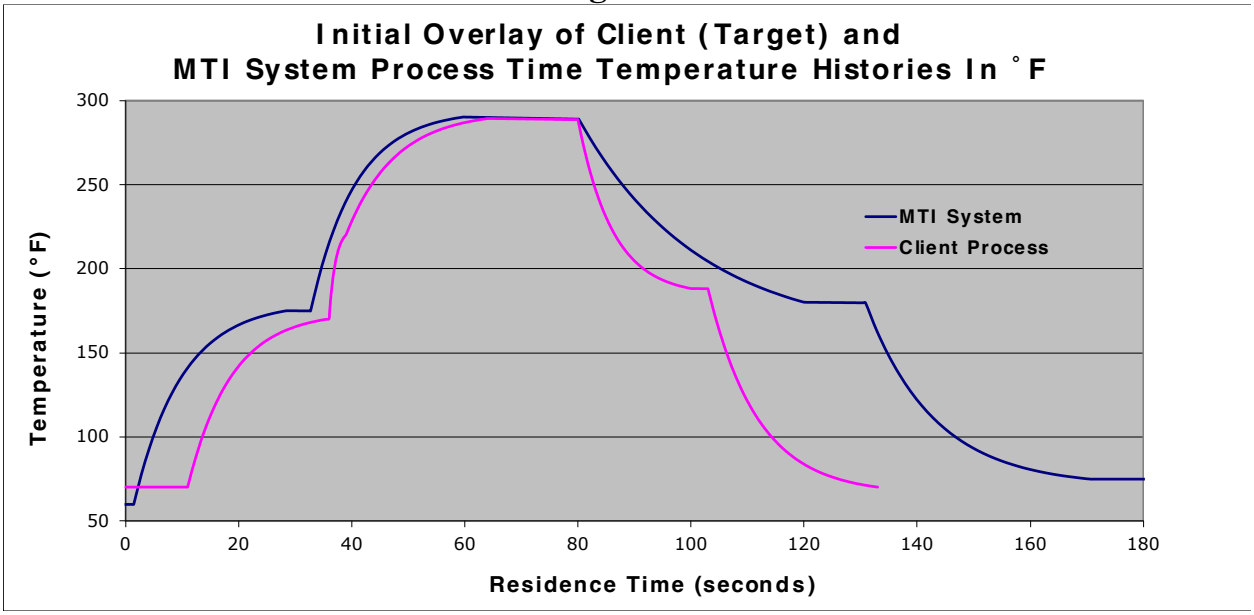
These data are very limited and do not represent the thermal exposure of the product as it flows through the heat exchangers because the product does not heat linearly. The process analysis is significantly improved using simulations based on the initial data to estimate the product temperature as it flows through the heat exchangers. These data produce a more realistic and accurate TTH of the commercial process. They are shown in Figure 2.0.

Figure 2



Now with the commercial process defined in good detail, a similar simulated TTH is developed based on their MTI BioScience ® System and the required process. We then overlay these two TTH graphs for comparison. This comparison is only the first step. See Figure 3.0 below.

Figure 3.

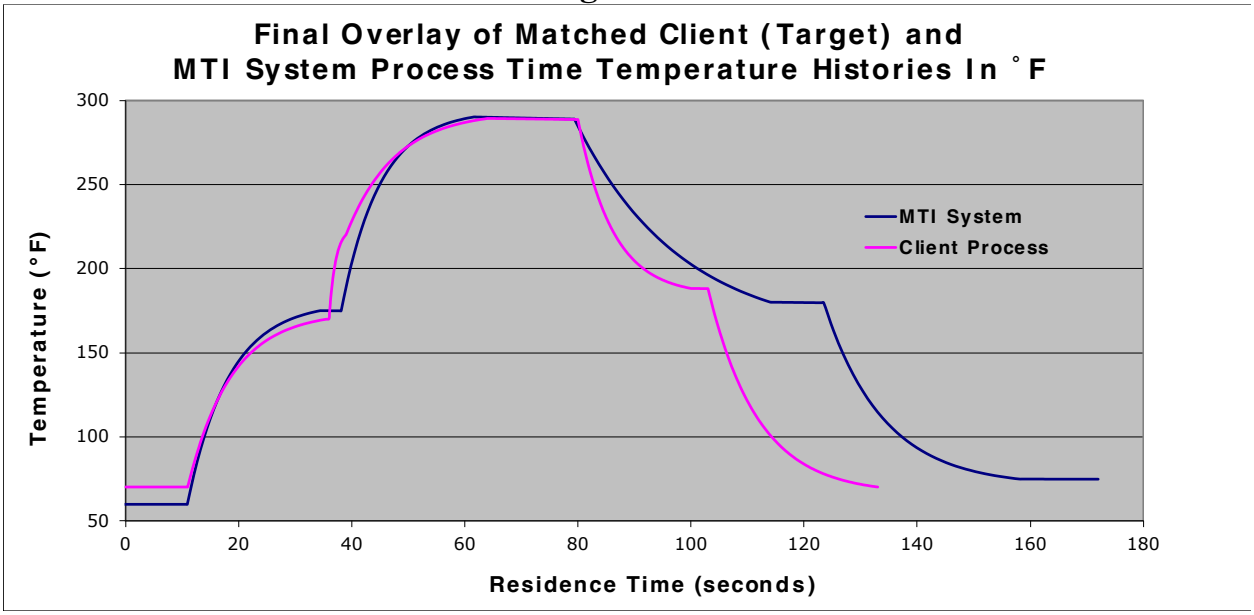


The agreement of the two TTHs is usually a reasonable first attempt but needs improvement. In this example, the hold times do not agree, and the MTI system's heating curve is too high. This means that if the laboratory system were operated under these conditions, the product would be greatly over-processed compared to the product from the client process.

To further improve the match of the processes, the operating conditions for the MTI system are changed repeatedly to produce the best agreement between the two TTHs. This, of course, is a subjective assessment leaving the question of the importance of the differences unanswered.

To evaluate this further (non-subjectively), we conduct a detailed analysis of the TTHs using our proprietary thermal process analysis methods and software. Using this analysis, we can assess the impact of the process conditions on the product's quality and the process's lethality. We then modify the analysis iteratively to select operating conditions for the research process that result in the best match to the client process. The resulting TTH overlay from this example is shown below in Figure 4.0.

Figure 4.0



Although the match between the two TTHs is not graphically perfect, it would be difficult and unnecessary to improve. The thermal process analysis indicates an excellent match, meaning that the areas of disagreement between the two graphs offset each other. To clarify, the areas where the client process is above the MTI BioScience system are offset by those where the client process is below the MTI BioScience system.

These differences are most important at temperatures above 250˚F (121˚C), where they significantly impact product quality. Conversely, areas below 250˚F (121˚C) are much more tolerant of differences between the two curves.

The final result is that the impact of the two processes is analytically the same and cannot be improved further. Our clients then use the final configuration and operating conditions we provide for the MTI BioScience system to match the impact of their production process in the laboratory with excellent success.