High pressure thermal processing offers potential to deliver safe, low-acid, chill-stable foods, with higher quality than traditional thermal processing as a result of reduced thermal exposure. Current industry guidelines suggest a thermal process with lethality (F) equivalent to 10 min at 90°C (i.e. \( F_{90^\circ C} 10 \text{ min} \)) to achieve the required 6-log reduction of spores of the target pathogen, non-proteolytic \textit{Clostridium botulinum} (NPCb). We compared the thermal-only (90°C) inactivation of seven NPCb strains in microbiological media and model foods (limited strains) to that achieved by lab-scale, HPT processes (600 MPa/90°C) to establish if HPT processing was at least as effective as thermal-only processing. The ‘Nanaimo’ strain was identified as highly heat and HPT resistant in comparison to the other strains. In microbiological media, approximately equivalent inactivation (~1.5 log cfu/g reduction) of ‘Nanaimo’ was achieved under thermal-only (\( F_{90^\circ C} 10 \text{ min} \)) and HPT (\( F_{90^\circ C} \approx 2 \text{ min} \)) conditions despite the HPT processes delivering ~5 times less thermal lethality. For the other strains, inactivation ranged from 3.0 to >5.8 and from 5.0 to >6.5 log cfu/g under similar thermal-only (\( F_{90^\circ C} 10 \text{ min} \)) and HPT (\( F_{90^\circ C} 2-3 \text{ min} \)) conditions, respectively. Our approach compared inactivation achieved by the processes on the basis of \( F_z \), assuming that the z-value was the same under thermal-only and HPT conditions. Hence, we further examined the kinetic inactivation of ‘Nanaimo’ under thermal-only and pilot-scale HPT (600 MPa) conditions, at four reference temperatures (82, 86, 90, 94°C). The observed z-values of 9.9 and 9.8°C, respectively, were not significantly different at the 95% confidence interval. These results demonstrate that assumptions regarding z-value are so far substantiated and that HPT processing can achieve greater, or at least equivalent, inactivation, whilst delivering much smaller thermal exposure, than by heat alone. Thus, HPT has the potential to offer significant quality benefits, while maintaining food safety assurance.