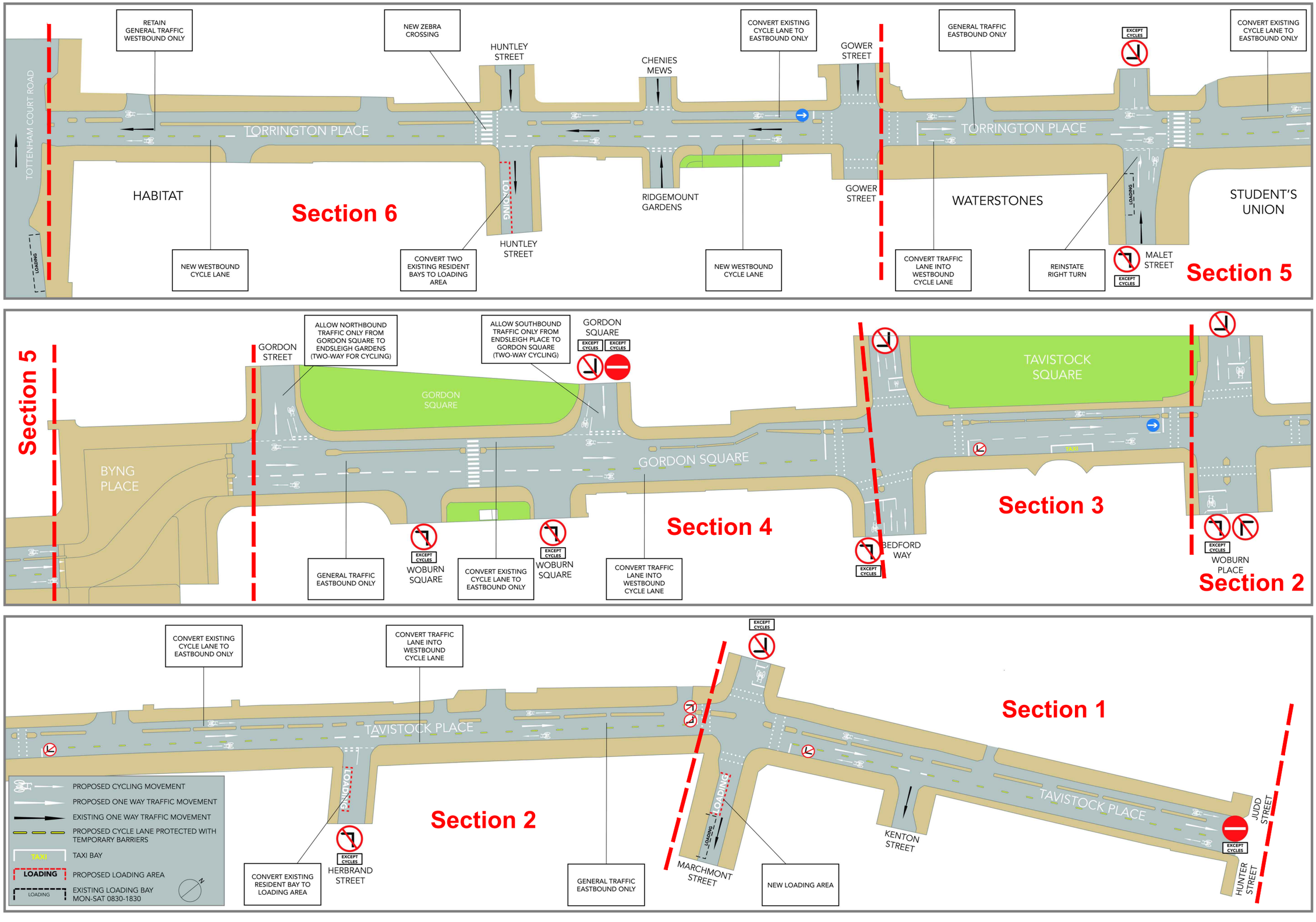Appendix 1: Illustration of the trial layout, showing sections where changes were introduced