The dynamics and depositional processes associated with block-and-ash flows (BAFs) are commonly inferred to be a function of granular flow, similar to debris flows and cold rock avalanches. Existing geophysical mass flow models are either based on frictional behavior (the Titan2D model) or another rheological law (i.e., a constant retarding stress), eventually adding some viscous and turbulent components (the VolcFlow model). The 2006 BAFs of Merapi present a rare opportunity to test these two models against a well-constrained field example. Integration of high-resolution field-based data into numerical simulations allows the validity of these models to be tested and rapid quantification of best-fit input parameters. We show that with the incorporation of spatially varying bed friction angles, Titan2D is capable of reproducing some characteristics of the 2006 Merapi flows over highly complex topography. Using a single free parameter, simulations obtained with VolcFlow also reproduce the morphology and distribution of the natural deposits. The results suggest that the performance of these models in simulating actual events is critically dependent on: (1) the calibration of the model by using extensive field-based data; (2) the incorporation of a suitable numerical topographic dataset; and (3) the choice of input parameters. Sensitivity analyses and inundation maps based on the probability of impact were used to produce a suite of potentially inundated areas from future BAFs affecting the southern flank of the volcano. Our results provide the basis for defining hazard zonations of key areas at risk from BAFs generating during future comparable eruptions at Merapi.