ABSTRACT
A wide range of clinical endpoints are commonly monitored in non-clinical models of acute radiation syndrome (ARS). The control group data from Rhesus monkeys that were included in multiple ARS studies (5.7 to 13 Gy) were compiled to assess the potential correlation between the incidence of diarrhea, decreased appetite, body weight changes and hematology parameters and clinical outcome. Body weight decreases (p<0.05) were significantly correlated with clinical outcome. A body weight decrease of ≥15% from baseline between Day 7 and Day 22 post-exposure was identified as a threshold for statistical significance and correlated with a negative outcome in 94.9% of the animals. Neutrophil (p<0.05) and platelet (p<0.05) nadirs were also significantly correlated with outcome. While each parameter was a significant predictor of clinical outcome when taken individually, a multiple regression analysis model that combined all significant parameters was superior to predict outcome. Although weight loss was a predictor of clinical outcome, the incidence of diarrhea and/or decreased appetite were not significant predictors of clinical outcome in this dataset. These results suggest that body weight changes and clinical pathology parameters can be useful predictors of clinical outcome in studies investigating the ARS model in Rhesus.

MATERIALS AND METHODS
All experimental procedures were performed in accordance with Institutional Animal Care and Use Committee (IACUC) and the Canadian Council on Animal Care guidelines for use of experimental animals. The data from 256 untreated Rhesus non-human primates (NHP) (187 preterminally fated and 69 survivors), either male or female, were compiled with their respective irradiation dose, day of death, body weights and hematology parameters. The animals were exposed to total body irradiation (Cobalt-60) at doses ranging between 5.7 and 13 Gy. All animals received at least minimal supportive care (opioid analgesic and fluid/nutritional support). The percentage of body weight loss was calculated relative to baseline. Blood platelet and neutrophil counts obtained with an automated analyzer (Advia 120). Survival curves are presented using the Kaplan-Meier function estimate.

RESULTS
A Log-Rank and two sided Tarone trend test were performed and indicated a correlation between body weight decrease and survival. A logistic regression was used to predict the mortality as a function of the weight lost, the lowest recorded neutrophil and platelet counts. The log transformed values was used for the neutrophil count. The logistic regression was performed for each parameter as well as including all parameters using a stepwise selection. The regression results indicated that each parameter as well as the combination of the three parameters can significantly predict the mortality.

DISCUSSION AND CONCLUSION
In animals exposed to TBI between 5.7 and 12 Gy, only 13 animals out of 256 survived despite a body weight decrease of 15% and greater (6.4%). The percent of survivors was 1.6% for animals with a body weight decrease reaching ≥20%. The Kaplan-Meier curve (Fig. 1) illustrates a correlation between the severity of the body weight and mortality in the Rhesus TBI ARS model. Platelet and neutrophil nadirs were also correlated with outcome. Neutropenia was correlated with increased incidence of infection. These results suggest that body weight changes and clinical pathology parameters can clinical outcome in the ARS model. This work was funded by BARDA (contract #s: HHS01002000060C, HHS010020100045C and HHS0100201000054C) and NIAID (contract #: HHSN27220130030C). These are the personal views of the individual authors and do not necessarily express the opinions or policies of the US Department of Health and Human Services or its components.