Red blood cells (RBCs) that are collected for transfusions and stored in PAGGSM can be kept for up to 42 days. Many changes accumulate in the RBCs during this time, but the most important one is the extent of the hemolysis, which determines whether the RBCs are suitable to be transfused. Cells from different donors decay at different rates, for reasons that have not been understood. A marker for this end-of-storage variability was identified by mass spectrometry, using red cell concentrates obtained from a regional quality control laboratory. Out of 636 units processed by this laboratory, 26 high hemolysis units (>0.5%) and 24 low hemolysis units (<0.15%) were assessed for end-of-storage lipid composition and cell morphology. The ratio of POPC (palmitoyl-oleoyl phosphatidylcholine) to SM (sphingomyelin) in the RBC membrane was significantly higher for samples from the high hemolysis donors. This was found to be because of the decrease of SM over the course of the storage period, which can be attributed to the action of sphingomyelinase. The hydrolysis products of SMs, ceramides, are well-known inducers of cell death, supporting the identification of the RBC lipid ratios as a marker of storage quality. The morphological analysis of the cells indicated that the lysis occurred via two different shape-changing pathways, and analysis of unfixed cells allowed the identification of the dynamic changes occurring during early stages of the transition away from the initial discocyte shape.