Understanding spaceflight risks to crew health and performance is a crucial aspect of preparing for exploration missions in the future. The research activities of the Human Research Program (HRP) provide substantial evidence to support most risk reduction work. The Human System Risk Board (HSRB), acting on behalf of the Office of Chief Health and Medical Officer (OCHMO), assesses these risks and assigns likelihood and consequence ratings to track progress. Unfortunately, many traditional approaches in risk assessment such as those used in the engineering aspects of spaceflight are difficult to apply to human system risks. This presentation discusses the unique aspects of risk assessment from the human system risk perspective and how these limitations are accommodated and addressed in order to ensure that reasonable inputs are provided to support the OCHMO’s overall risk posture for manned exploration missions.