

HZV Reactivation CLIFF Peer Review

1. *Strength of evidence presented in CLIFF in modeling the characteristics and mission impact of this medical condition within the spaceflight environment?*

Score: 3

Grading Scale:

4 - *Confident*

3 - *Somewhat confident*

2 – *Neutral*

1 – *Somewhat unconfident*

0 – *Not confident*

2. How confident are you that these data accurately represent the spaceflight environment?	Tables 1, 2 Composite Incidence and Level of Confidence	Table 3, 4 BC/WC Loss of Crew and probability	Table 4 - Clinical Phase 1, 2 durations Table 5 – CP 2 Loss of Crew	Table 4 – RTDC % Table 6 – RTDC Loss of Crew	Table 4 – Loss of Crew Life % Table 7 – Loss of Crew Life, Loss of Crew	Table 8 – TI
Score	3	3	3	2	3	3

Note: Tab 9B needs the graphical incidence distribution.

Comments and limitations:

1. **General comments.** Herpes zoster (HZV) is caused by the varicella virus which can remain latent in the dorsal root ganglia for years and then be reactivated in adults who had a primary infection (chickenpox) in their youth. It can cause a self-limited infection that, while uncomfortable, usually only causes a rash in a single dermatomal distribution. More invasive infections can result in meningoencephalitis, involvement of the auditory and visual systems, and a widely disseminated rash. Facial involvement can result in post-herpetic neuralgia that can last for months or even years. There is laboratory evidence that astronauts may be more at risk due to a compromised immune system, potentially from the stress of spaceflight and the spaceflight environment itself. There have been no reported cases of herpes zoster during spaceflight.

2. **Incidence.** Since there are no reports of HZV reactivation during spaceflight, terrestrial data was used to calculate the composite incidence. A manuscript by Reyes, et al., was chosen to be the source of incidence data since it used a similar population to astronauts in an analog environment.

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Two papers showed up to a 10 times higher risk for reactivation in analog populations, possibly due to increased stress compared with the general population. I agree that this is the best data that we can utilize to estimate the risk. It should be noted that vaccination in astronauts older than 50 years could be considered as a preventative strategy and possibly in astronauts younger than 50 if the higher risk of reactivation in space outweighs the risk of vaccination. The best case/worst case probability calculation was difficult due to the protean manifestations and complications of HZV. Using averaged terrestrial data, a rational estimate of WC probability of 20% was obtained. Clinical durations, RTDC and Loss of crew life probabilities are supported by terrestrial evidence. The probability density curve that was derived appears to be a reasonable representation of the data presented.

3. Clinical phase data. I am in agreement with the clinical phase 1 duration entered in this CLIFF. This data was compiled by a team of expert clinicians, and I was involved in the discussions leading to the calculation of the clinical phase duration. I am also in agreement with CP2 duration specified.

4. Task impairment. The analysis was performed and reviewed by a separate team of expert clinicians. I am aware of the methods that were used but did not directly participate in the discussions.

5. Dependence on mission phase or duration of mission. This medical condition should not be dependent on mission phase as reactivation could occur at any time..

6. Limitations

- Once an episode occurs, the incidence of further cases will likely increase significantly. This is true because HAV is a highly contagious virus and adequate protective gear may not be available on board. Also, once an individual has a case of reactivation, his/her risk of another case increases.
- The use of HZV vaccination for those eligible can decrease the risk of infection and affect the incidence calculation.
- The composite incidence would predict a case of HZV reactivation within 33 person-years of spaceflight. There have been no reports of a case in nearly 50 person-years to date.
- The worst case includes many of the complications from HZV, but not all of them (e.g., encephalitis). Each of these complications are unique and have different durations. This made defining an “average” worst case problematic.

Reviewed by:

David C. Hilmers