

Eye Irritation Corneal abrasion and ulceration 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: 2

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	2	3	3	3	3	3

Comments and limitations:

1. General comments. This CLIFF covers a wide range of eye problems, ranging from minor irritation to sight-threatening corneal ulceration. Because of microgravity, the cabin environment may have a significant number of suspended particles (food, liquids, dust, etc) which can cause ocular irritation or abrasion. In addition, research shows a possible slowing in the blink rate, lower cabin humidity and changes in the tear film layer in microgravity, all of which could predispose to injury to the eye. Specific conditions that are covered in this CLIFF are eye irritation, dry eye, foreign bodies, abrasion, corneal ulceration, chemical burns and idiopathic etiologies. It is well-documented that individuals who wear contact lenses are at increased risk for abrasions, ulcerations, and microbial pathogens. Therefore, it was necessary to create a separate distribution for those who wear contacts. There have been 96 reported cases in spaceflight that fit the definition of this CLIFF; however, none of them fit the worst case definition of corneal ulceration or required surgery.

2. Incidence. The broad definition of this CLIFF created challenges in finding studies that specifically investigated the conditions included. There is fairly robust spaceflight data available in two overlapping reports. However, the events reported were not easily categorized, the percentage

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of contact lens wearers was not available, and reconciliation between the reports needed to be accomplished. A baseline incidence rate was calculated from available spaceflight data which can be applied to all crewmembers. Another distribution was made that covers the additional risk for abrasion and ulceration in contact wearers; this was derived from terrestrial and analog sources. While the resulting distributions are supported by the available evidence, there are concerns for underestimation of the risk to contact lens wearers. For example, the incidence of corneal abrasion in contact lens wearers should be more common than the much more serious corneal ulceration. Yet, the rate of ulceration that is derived from terrestrial sources shows an incidence that is about 50% higher than abrasions. The numbers also imply that there is little additional risk for contact lens wearers. The total incidence rate calculated for contact lens wearers is 2.112 while it is 2.108 for non-contact lens wearers. Intuitively, one would think that the relative risk of eye complications would be higher than this in contact lens wearers. Improvements in contact lens technology need to be recognized that might mitigate this risk. The best case/worst case (corneal ulceration or the need for surgery) probability was specified as a range of values. The highest best-case probability/lowest worst case probability of 99.5%/0.5% was based on subject matter expert opinion given that no worst case events have occurred in 96 spaceflight reports. The lower limit of best-case probability was calculated as 96% from terrestrial studies which is felt to be an overestimate of worst case events, given the available spaceflight data. The clinical phase durations, RTDC and Loss of crew life probabilities are supported by terrestrial evidence, and I am in agreement with their calculation. The probability density curve that was derived for baseline incidence appears to be a reasonable representation of the data presented. The distribution that describes the incidence rate for contact lens wearers may have a variance that overstates the confidence that we have in this incidence rate.

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. CP2 was supported by terrestrial evidence.

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 may be dependent on mission phase, particularly in partial g environments where the hazard of suspension of particles in the living environment will be reduced.

6. Limitations

- The definitions for this condition were confusing as they overlapped with other ocular definitions (i.e. corneal ulceration is typically infectious in nature and there is an existing anterior eye infection CLIFF).
- There was no spaceflight data available to calculate incidence related to contact lenses use.
- The ocular definitions were updated in this effort without a concomitant LSAH pull.
- Literature regarding the untreated worst-case scenario was extremely limited and several parameters are based on subject matter expert opinion.
- While the resulting distributions are supported by the evidence, there are concerns for underestimation of the risk to contact lens wearers. For example, the incidence of corneal abrasion in contact lens wearers should be more common than the much more

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serious corneal ulceration. Yet, the rate of ulceration that is derived from terrestrial sources shows an incidence that is about 50% higher than abrasions.

- The incidence rates imply that there is little additional risk for contact lens wearers. The total incidence rate calculated for contact lens wearers is 2.112 per person-year while it is 2.108 for non-contact lens wearers. Intuitively, one would think that the relative risk of eye complications would be higher than this in contact lens wearers.
- Because of their large sample size, the studies used to compute the composite incidence of risk in contact lens wearers most likely overestimates the confidence we have in the assigned value.
- This medical condition may be dependent on mission phase, particularly in partial g environments where the hazard of suspension of particles in the air will be reduced.
- Under-reporting for this condition could have been present during past space missions due to subtle eye irritation that may not have been reported by the crew.

Reviewed by:

David C. Hilmers