

**IMPORTANT SERVICE REQUEST NOTICE (S-20170724-387)**

*This service report should not be used for diagnostic or treatment decisions, which are outside the scope of the model. Please include the service request number (S-20170724-387) on any presentations or documentation referencing this service request.*

## Executive Summary

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In order to help quantify the impact of sex differences on medical outcomes during deep space missions, 3 different deep space mission duration times (42, 182, and 913 days) with No EVAs were modeled for 3 crew profiles:

- Mixed sex crew (2 males, 2 females) [DRMs 1, 2, 3]
- All female crew [DRMs 4, 5, 6]
- All male crew [DRMs 7, 8, 9]

There are currently 20 sex-dependent conditions in the IMM Medical Condition List (IMCL). Of these, 9 occur in greater frequency in males, and 11 in females. Urinary Tract Infection (which has a higher female than male incidence) is the only sex-dependent condition in the top 5 ranked influential conditions for EVAC.

**Sex dependent differences in medical outcomes were found. The differences between male and female probability of EVAC is most apparent in the 913 day mission than in the shorter duration missions. Females have higher rates of evacuation (EVAC) during the 913 day (2.5 year) DRM. Details of the model results are delineated further in the report that follows.**

## Background

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The IMM is a stochastic model that uses Monte Carlo methodology to simulate medical outcomes during spaceflight missions. The IMM consists of a three-step process. First, mission and crew member characteristics are specified to define a particular mission profile, or design reference mission (DRM). Next, medical events and outcomes during the space flight mission are randomly generated based on pre-defined incidence values and probability distributions. Finally, total crew health and mission impact outcomes are summarized. For this report, the primary outcomes of interest are crew health index (CHI), need for evacuation (EVAC) and loss of crew life (LOCL).

The IMM is most useful for comparing risks across multiple mission profiles based on probable events and resource availability. Biased results may be incurred due to limitations of the model, but the bias will be consistent across mission profiles within the same service request.

## Methods

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### Crew and Mission Parameters

The DRMs were configured using the crew profiles shown in Tables 1, 2 and 3. The outcomes of certain IMM medical conditions are influenced by pre-existing medical history including: coronary artery calcium score (CAC), dental crowns, contact lenses, and history of prior abdominal surgery. Pre-existing conditions, as defined here, are consistent with historical U.S. crew data. CAC was specified as positive in one male, and in no female crew members, which is also consistent with historical crew data. For this request, the customer specified that none of the DRMs include EVAs. Currently, there are no sex-dependent EVA-related conditions in the Integrated Medical Evidence Database (iMED).

**Table 1. Mixed Sex Crew for DRMs 1, 2 and 3 (42, 182 and 913 days respectively)**

| Crew Member | Sex    | CAC | Crowns | Contacts | Prior Abdominal Surgery | EVA |
|-------------|--------|-----|--------|----------|-------------------------|-----|
| Crew 1      | Male   | Yes | Yes    | No       | No                      | No  |
| Crew 2      | Male   | No  | No     | Yes      | Yes                     | No  |
| Crew 3      | Female | No  | Yes    | No       | No                      | No  |
| Crew 4      | Female | No  | No     | Yes      | No                      | No  |

**Table 2. All Female Crew for DRMs 4, 5 and 6 (42, 182 and 913 days respectively)**

| Crew Member | Sex    | CAC | Crowns | Contacts | Prior Abdominal Surgery | EVA |
|-------------|--------|-----|--------|----------|-------------------------|-----|
| Crew 1      | Female | No  | Yes    | No       | No                      | No  |
| Crew 2      | Female | No  | No     | Yes      | Yes                     | No  |
| Crew 3      | Female | No  | Yes    | No       | No                      | No  |
| Crew 4      | Female | No  | No     | Yes      | No                      | No  |

**Table 3. All Male Crew DRMs 7, 8 and 9 (42, 182 and 913 days respectively)**

| Crew Member | Sex  | CAC | Crowns | Contacts | Prior Abdominal Surgery | EVA |
|-------------|------|-----|--------|----------|-------------------------|-----|
| Crew 1      | Male | Yes | Yes    | No       | No                      | No  |
| Crew 2      | Male | No  | No     | Yes      | Yes                     | No  |
| Crew 3      | Male | No  | Yes    | No       | No                      | No  |
| Crew 4      | Male | No  | No     | Yes      | No                      | No  |

### Medical Conditions and Resources

The one hundred medical conditions currently included in the IMM are shown in Appendix A. The incidence of IMM medical events occurring during simulated missions are based on historical mission and cohort data contained within the iMED. For each condition the percentage of “best case” and “worst case” scenarios are specified, as well as a defined set of medical resources that are used to treat the condition. The iMED entry for each condition details the specific medical resources and quantity necessary for treatment in both the best and worst-case scenarios. In-flight medical treatment is assumed to follow a specified protocol [5] or clinical practice guidelines for each medical condition and is constrained by resource availability on the ISS (i.e. the ISS medical capabilities (MedCap)). Model outcomes can be given for the all-treated (continuous resupply, e.g. ISS in low earth orbit), all-untreated (no Medkit) and baseline MedCap (ISS Medkit without resupply). For this service request only the MedCap state was utilized, because this should most closely resemble a real world deep space mission where resupply is not possible but where utilization of partial and alternative treatment can occur.

The iMED contains 20 conditions with sex specific incidence, as shown in Table 4 below. Of these, 9 occur in greater frequency in males, and 11 in females. Three of these conditions apply solely to females (urinary incontinence, vaginal yeast infection, and abnormal uterine bleeding), while one applies solely to males (prostatitis). Of the 5 trauma-related conditions in the list (hip/femur fracture, lumbar spine fracture, lower extremity fracture, compartment syndrome, and retinal detachment), males have higher incidence rates in 4 of the 5 conditions (female incidence is higher with lower extremity fracture). All remaining conditions of the 20 listed in Table 4 are categorized as those related to medical illness. Two of the medical illness-related conditions are associated with space adaptation, including urinary incontinence, which is female only, and urinary retention, where females have a higher incidence than males. There is no difference in the incidence of EVA-related conditions for males or females.

**Table 4. Sex dependent Conditions in the iMED Database**

*Note: Blue shading indicates higher incidence in males, pink/salmon shading indicates higher incidence in females. Trauma conditions are bolded.*

| Medical Condition                 | Category      | Space Adaptation | Higher In... |
|-----------------------------------|---------------|------------------|--------------|
| ACUTE PROSTATITIS                 | Medical       | No               | Males only   |
| ABNORMAL UTERINE BLEEDING         | Medical       | No               | Females only |
| URINARY INCONTINENCE              | Medical       | Yes              | Females only |
| VAGINAL YEAST INFECTION           | Medical       | No               | Females only |
| ACUTE ARTHRITIS                   | Medical       | No               | Females      |
| ACUTE CHOLECYSTITIS/BILIARY COLIC | Medical       | No               | Females      |
| ACUTE COMPARTMENT SYNDROME        | <b>Trauma</b> | No               | Males        |

| Medical Condition                                    | Category | Space Adaptation | Higher In... |
|------------------------------------------------------|----------|------------------|--------------|
| ACUTE GLAUCOMA                                       | Medical  | No               | Females      |
| ANGINA/MYOCARDIAL INFARCTION                         | Medical  | No               | Males        |
| ANXIETY                                              | Medical  | No               | Females      |
| ATRIAL FIBRILLATION/ ATRIAL FLUTTER                  | Medical  | No               | Males        |
| CARDIOGENIC SHOCK SECONDARY TO MYOCARDIAL INFARCTION | Medical  | No               | Males        |
| DEPRESSION                                           | Medical  | No               | Females      |
| HIP/PROXIMAL FEMUR FRACTURE                          | Trauma   | No               | Males        |
| LOWER EXTREMITY (LE) STRESS FRACTURE                 | Trauma   | No               | Females      |
| LUMBAR SPINE FRACTURE                                | Trauma   | No               | Males        |
| RETINAL DETACHMENT                                   | Trauma   | No               | Males        |
| STROKE (CEREBROVASCULAR ACCIDENT)                    | Medical  | No               | Males        |
| URINARY RETENTION                                    | Medical  | Yes              | Females      |
| URINARY TRACT INFECTION                              | Medical  | No               | Females      |

## Main Outcomes

The IMM primary medical outcomes include: total medical events (TME), crew health index (CHI), probability of Evacuation (EVAC), probability of Loss of Crew Life (LOCL), and required resources.

CHI is a calculated percentage using the quality-adjusted mission time lost (QAMTL) due to in-flight medical events and resources available to treat those conditions [2].

$$\text{CHI (\%)} = [ 1 - ( \text{QAMTL} \div \text{Mission Length} ) ] \times 100$$

For a given condition, QAMTL is determined by summing the product of functional impairment and duration for all three clinical phases of that condition: i) diagnosis and initial treatment, ii) ongoing treatment, and iii) end-state. CHI percent values range from 0-100, where zero represents complete crew impairment and one hundred represents a completely functional crew.

EVAC in the context of IMM means that medical evacuation from the ISS would be considered for definitive treatment of the afflicted crew member(s). EVAC is considered an end state result if any of the following criteria are met: 1) potential LOCL; 2) potential significant permanent impairment; or 3) potential intractable pain. When EVAC is calculated by the IMM, no consideration has been given to the

availability of a return vehicle or the likelihood of a successful clinical outcome should a return vehicle be available.

LOCL in the context of IMM should be interpreted to mean that the clinical scenario resulted in death of the affected crew member(s). In version 4.1 of the IMM, crew members are usually only assigned one end state of EVAC or LOCL. In rare instances a crewmember can get a condition that will go to EVAC or LOCL, and then develop another condition that will also go to EVAC or LOCL in the time between the onset of first condition and the EVAC or LOCL time. Both events are recorded as EVAC or LOCL outcomes. These assumptions should result in more accurate IMM forecasts for the occurrence of EVAC and LOCL as compared to the prior versions of the model.

Required resources for treatment are tracked for each simulated mission trial. The number of each resource that is used to treat a given condition is decremented from available resources. If more of any particular resource is used than is available, then that resource is considered “depleted” in the MedCap scenario. Events that require a “depleted” resource are considered “partially treated” if only a portion of the required resources are available. If there are sufficient available alternate resources in the MedCap, the event is considered “fully treated.” If there are not enough resources available to treat the event, the event is considered “untreated.” The initial quantities for medical resources are baselined to a fully stocked ISS medical kit (MedCap).

### Modeling Approach

Simulations were run for a 42 day (lunar sortie), 183 day (6 month, ISS) and 193 day (2.5 year, Mars) missions using the crew profiles shown above. One hundred thousand (100,000) trials were run for each DRM where each trial can be considered an individual “mission”. This ensures that the distribution of outcomes meet convergence criteria. Convergence criteria are met when there is less than or equal to a 5% change in the average standard deviation of the CHI, EVAC, and LOCL primary model outcomes in the last 2 - 1,000 mission increments. This last step is performed manually by the modelers using the IMM V4 Convergence Report.

IMM outcomes were determined for the DRMs using the ISS MedCap scenario where all conditions are treated, partially treated or untreated based on the available resources of the ISS MedCap. CHI is calculated as a percentage, with 95% confidence intervals (CIs) for the associated distributions. EVAC and LOCL are probabilities, with 95% CI for EVAC and LOCL obtained using bootstrap resampling of the simulation output [3]. In this report, CHI, EVAC and LOCL results, as well as pertinent influential conditions, are described. IMM version 4.1 has certain features, assumptions and limitations that impact modeled outcomes. IMM 4.1 represents a significant advance over IMM 3.0. Improvements in IMM 4.1 include inclusion of a timeline, and alternate or partial treatment capability. Features, assumptions and limitations pertinent to this report are described below.

### Features, Assumptions and Limitations of IMM Version 4.1 [3]

1. All non-SA and non-extravehicular activity (EVA) related conditions have a uniform likelihood of occurring throughout the mission duration. Space Adaptation Syndrome conditions occur in the first 5 days of the mission, with a peak occurrence at 48 hours.

2. Individuals cannot get the same condition for which they are currently being treated (i.e. during Clinical Phase (CP) I and II).
3. EVAC and LOCL are generated for each medical event, and then the timing of the EVAC or LOCL is generated according to a specified distribution.
4. Individuals are no longer at risk for further conditions once their status changes to either EVAC or LOCL. From the start time of the EVAC or LOCL, the functional impairment of the crew member is assumed to be 100%.
5. When the status of a crew member changes to EVAC, only one crew member is evacuated.
6. The IMM assumes that, per crew member, the first condition requiring a specific therapy utilizes all resources required for treating that condition before a second condition has access to those resources.
7. Most medical conditions, with exceptions including acute radiation syndrome and EVA-linked conditions, occur independently of the occurrence of mission events and other medical conditions. Currently there is no correlation or association within or between crew members for most medical conditions.
8. The model assumes another crew member is available to act as caregiver but does not track the time impact of providing this care.
9. Medical procedures are accurately followed and successful; no mistakes occur in executing medical procedures.
10. Crew medical skill level and preflight/inflight training is not modeled.
11. All diagnoses are 100% accurate.
12. All pharmaceuticals maintain maximum efficacy.
13. All medical events receive the appropriate treatment.
14. All medical events respond to the treatment as expected terrestrially.
15. All medical equipment is 100% reliable.
16. For each of the medical conditions specified in iMED, all crew members with the same characteristics (sex, presence of CAC, crowns, contacts, history of abdominal surgery) have the same likelihood distribution of experiencing the condition.
17. All crew members are assumed to have all intrinsic body parts intact (i.e. appendix, gall bladder, and uterus or prostate, etc.).
18. IMM assumes ISS power, potable water and oxygen resources are always available in unlimited supply.
19. No Russian medical capabilities aboard the ISS are available to US crew members in this model.
20. Medical capabilities do not include the use of personal crew carry-on items contained in the Individual Medical Accessories Kit, (IMAK).
21. If a crew member is undergoing treatment for concurrent medical conditions requiring the same consumable resource, the crew member will only utilize resources at the level required by the condition that requires the most resources.

22. If the primary resource required for treating a medical condition is unavailable, one or more alternative resources are considered, if appropriate. One example might be using acetaminophen in place of ibuprofen.

23. Total quantities of a consumable medical resource requiring a daily dose will be adjusted if a dosage schedule runs past the end of the mission.

24. If a solar particle event causes acute radiation sickness in one or more crew members, IMM assumes the condition begins identically in all affected crew members at the beginning of the solar particle event.

25. The IMM does not decrement non-consumable items and allows all non-consumable items to be used simultaneously by multiple astronauts (e.g. blood pressure cuff).

## Results

The IMM results for CHI, EVAC and LOCL for the simulated DRMs are presented in the figures and tables below. Figure 1 and Table 5 show CHI across all DRMs. Decline in CHI with increasing mission length is caused by eventual depletion of MedCap resources.

### Crew Health Index (CHI) Results

**Figure 1: Crew Health Index (CHI), All DRMs**

*Error bars are the 95% confidence interval.*

**Table 5. CHI (%), All DRMs**

| DRM / Mission Profile   | Treatment Scenario | Mean CHI (%) | 95% CI Lower | 95% CI Upper |
|-------------------------|--------------------|--------------|--------------|--------------|
| DRM 1 (42d, Mixed Sex)  | MedCap             | 97.36        | 92.86        | 98.99        |
| DRM 1 (42d, Mixed Sex)  | Treated            | 97.35        | 92.81        | 98.99        |
| DRM 1 (42d, Mixed Sex)  | Untreated          | 86.11        | 65.19        | 94.77        |
| DRM 2 (182d, Mixed Sex) | MedCap             | 94.99        | 81.10        | 98.81        |
| DRM 2 (182d, Mixed Sex) | Treated            | 95.01        | 81.25        | 98.82        |
| DRM 2 (182d, Mixed Sex) | Untreated          | 60.07        | 40.01        | 74.06        |
| DRM 3 (913d, Mixed Sex) | MedCap             | 80.87        | 63.03        | 91.34        |
| DRM 3 (913d, Mixed Sex) | Treated            | 89.01        | 70.38        | 96.79        |
| DRM 3 (913d, Mixed Sex) | Untreated          | 19.27        | 11.32        | 26.58        |
| DRM 4 (42d, All Female) | MedCap             | 97.25        | 92.73        | 98.95        |

| DRM / Mission Profile    | Treatment Scenario | Mean CHI (%) | 95% CI Lower | 95% CI Upper |
|--------------------------|--------------------|--------------|--------------|--------------|
| DRM 4 (42d, All Female)  | Treated            | 97.25        | 92.68        | 98.95        |
| DRM 4 (42d, All Female)  | Untreated          | 84.65        | 62.56        | 94.54        |
| DRM 5 (182d, All Female) | MedCap             | 94.83        | 81.06        | 98.72        |
| DRM 5 (182d, All Female) | Treated            | 94.89        | 81.27        | 98.73        |
| DRM 5 (182d, All Female) | Untreated          | 58.57        | 37.05        | 73.37        |
| DRM 6 (913d, All Female) | MedCap             | 78.57        | 60.34        | 89.67        |
| DRM 6 (913d, All Female) | Treated            | 88.70        | 70.20        | 96.49        |
| DRM 6 (913d, All Female) | Untreated          | 18.51        | 10.39        | 25.83        |
| DRM 7 (42d, All Male)    | MedCap             | 97.47        | 93.08        | 99.03        |
| DRM 7 (42d, All Male)    | Treated            | 97.46        | 93.05        | 99.03        |
| DRM 7 (42d, All Male)    | Untreated          | 87.58        | 69.19        | 95.06        |
| DRM 8 (182d, All Male)   | MedCap             | 95.13        | 81.23        | 98.89        |
| DRM 8 (182d, All Male)   | Treated            | 95.13        | 81.30        | 98.89        |
| DRM 8 (182d, All Male)   | Untreated          | 61.62        | 43.15        | 74.83        |
| DRM 9 (913d, All Male)   | MedCap             | 82.56        | 65.18        | 92.42        |
| DRM 9 (913d, All Male)   | Treated            | 89.33        | 70.68        | 97.06        |
| DRM 9 (913d, All Male)   | Untreated          | 20.10        | 12.28        | 27.37        |

### Need for Evacuation (EVAC) Results

Figure 2 shows that the all-female crew had a higher rate of consideration for EVAC. Two conditions with higher female incidence rates (Urinary Tract Infection and Lower Extremity Stress Fractures) were among the top influential conditions for EVAC in the all-female crew scenario (as seen in Table 7). These two conditions are partially treated worst-cases.

For Urinary Tract Infection, the worst-case treated outcome has bounds of 0 – 1% on the probability of EVAC, while the worst-case untreated outcome has bounds of 0 – 100% on the probability of EVAC. These bounds are used in the model to determine the probability of EVAC for the condition during each trial of the simulation. In IMM 4.1, partial treatment scales between treated and untreated outcomes based on an EVAC distribution using the minimum and maximum probability as bounds. For partial treatment, weighted averages of the minimum and maximum using the fully treated and untreated

bounds are calculated, and those averages are used as bounds for the partially treated EVAC distribution.

**Figure 2: Need for Evacuation (EVAC), All DRMs**

*Error bars are the 95% confidence interval.*

**Table 6. EVAC Probability, All DRMs**

| DRM / Mission Profile    | Treatment Scenario | EVAC Probability | 95% CI Lower | 95% CI Upper |
|--------------------------|--------------------|------------------|--------------|--------------|
| DRM 1 (42d, Mixed Sex)   | MedCap             | 0.0103           | 0.0097       | 0.0110       |
| DRM 1 (42d, Mixed Sex)   | Treated            | 0.0101           | 0.0095       | 0.0108       |
| DRM 1 (42d, Mixed Sex)   | Untreated          | 0.2030           | 0.2005       | 0.2054       |
| DRM 2 (182d, Mixed Sex)  | MedCap             | 0.0365           | 0.0352       | 0.0377       |
| DRM 2 (182d, Mixed Sex)  | Treated            | 0.0329           | 0.0317       | 0.0341       |
| DRM 2 (182d, Mixed Sex)  | Untreated          | 0.5126           | 0.5096       | 0.5158       |
| DRM 3 (913d, Mixed Sex)  | MedCap             | 0.2954           | 0.2925       | 0.2983       |
| DRM 3 (913d, Mixed Sex)  | Treated            | 0.1122           | 0.1104       | 0.1142       |
| DRM 3 (913d, Mixed Sex)  | Untreated          | 0.9599           | 0.9587       | 0.9611       |
| DRM 4 (42d, All Female)  | MedCap             | 0.0099           | 0.0093       | 0.0106       |
| DRM 4 (42d, All Female)  | Treated            | 0.0096           | 0.0091       | 0.0103       |
| DRM 4 (42d, All Female)  | Untreated          | 0.2541           | 0.2515       | 0.2572       |
| DRM 5 (182d, All Female) | MedCap             | 0.0388           | 0.0377       | 0.0401       |
| DRM 5 (182d, All Female) | Treated            | 0.0312           | 0.0301       | 0.0323       |
| DRM 5 (182d, All Female) | Untreated          | 0.5536           | 0.5506       | 0.5569       |
| DRM 6 (913d, All Female) | MedCap             | 0.3504           | 0.3473       | 0.3534       |
| DRM 6 (913d, All Female) | Treated            | 0.1102           | 0.1082       | 0.1122       |
| DRM 6 (913d, All Female) | Untreated          | 0.9678           | 0.9666       | 0.9688       |
| DRM 7 (42d, All Male)    | MedCap             | 0.0107           | 0.0101       | 0.0114       |
| DRM 7 (42d, All Male)    | Treated            | 0.0106           | 0.0100       | 0.0112       |
| DRM 7 (42d, All Male)    | Untreated          | 0.1496           | 0.1474       | 0.1520       |

| DRM / Mission Profile  | Treatment Scenario | EVAC Probability | 95% CI Lower | 95% CI Upper |
|------------------------|--------------------|------------------|--------------|--------------|
| DRM 8 (182d, All Male) | MedCap             | 0.0354           | 0.0343       | 0.0365       |
| DRM 8 (182d, All Male) | Treated            | 0.0334           | 0.0323       | 0.0345       |
| DRM 8 (182d, All Male) | Untreated          | 0.4676           | 0.4644       | 0.4705       |
| DRM 9 (913d, All Male) | MedCap             | 0.2284           | 0.2258       | 0.2311       |
| DRM 9 (913d, All Male) | Treated            | 0.1158           | 0.1138       | 0.1178       |
| DRM 9 (913d, All Male) | Untreated          | 0.9495           | 0.9481       | 0.9508       |

In DRM6, for the all-female crew, sex dependent conditions of Urinary Tract Infection and Lower Extremity Stress Fracture account for 20.4% of EVAC events, as shown in Table 7. For the all-male crew (DRM9), the only sex dependent condition is Hip/Proximal Femur Fracture, which accounts for 1.51% of all EVAC events and does not appear in the influential conditions list until rank #19 for the all-male crew. Table 8 shows the top ten influential conditions for DRM9.

**Table 7. Influential Conditions for EVAC, 913 day DRM6, Female Only Crew**

*Note: Conditions #2 and #10 are sex dependent in the model and have higher model incidence rates of occurrence in females.*

| # | Scenario   | Treated | Medical Condition                                               | Category    | Total EVAC | % Contrib. | Cum. % |
|---|------------|---------|-----------------------------------------------------------------|-------------|------------|------------|--------|
| 1 | BEST CASE  | PARTIAL | EYE CHEMICAL BURN                                               | ENVIRONMENT | 11702      | 28.45      | 28.45  |
| 2 | WORST CASE | PARTIAL | URINARY TRACT INFECTION                                         | MEDICAL     | 7710       | 18.74      | 47.19  |
| 3 | WORST CASE | PARTIAL | BACK SPRAIN/STRAIN                                              | TRAUMA      | 2088       | 5.08       | 52.27  |
| 4 | WORST CASE | PARTIAL | EYE CHEMICAL BURN                                               | ENVIRONMENT | 1877       | 4.56       | 56.83  |
| 5 | BEST CASE  | PARTIAL | FINGER DISLOCATION                                              | TRAUMA      | 1527       | 3.71       | 60.54  |
| 6 | WORST CASE | PARTIAL | NEPHROLITHIASIS                                                 | MEDICAL     | 1124       | 2.73       | 63.28  |
| 7 | WORST CASE | TREATED | VISUAL IMPAIRMENT AND/OR INCREASED INTRACRANIAL PRESSURE (VIIP) | MEDICAL     | 1026       | 2.49       | 65.77  |

| #  | Scenario   | Treated | Medical Condition               | Category    | Total EVAC | % Contrib. | Cum. % |
|----|------------|---------|---------------------------------|-------------|------------|------------|--------|
| 8  | WORST CASE | TREATED | SMOKE INHALATION                | ENVIRONMENT | 668        | 1.62       | 67.39  |
| 9  | WORST CASE | PARTIAL | EYE INFECTION                   | MEDICAL     | 617        | 1.50       | 68.89  |
| 10 | WORST CASE | PARTIAL | LOWER EXTREMITY STRESS FRACTURE | TRAUMA      | 534        | 1.30       | 70.19  |

**Table 8. Influential Conditions for EVAC, 913 day DRM9, Male Only Crew**

*Note: No sex dependent conditions appear until condition rank #19 (Hip/Proximal Femur Fracture, 382 trials, 1.51% contribution).*

| #  | Scenario   | Treated | Medical Condition                                                                 | Category    | Total EVAC | % Contrib. | Cum. % |
|----|------------|---------|-----------------------------------------------------------------------------------|-------------|------------|------------|--------|
| 1  | BEST CASE  | PARTIAL | EYE CHEMICAL BURN                                                                 | ENVIRONMENT | 4072       | 16.08      | 16.08  |
| 2  | WORST CASE | PARTIAL | BACK SPRAIN/STRAIN                                                                | TRAUMA      | 2033       | 8.03       | 24.10  |
| 3  | BEST CASE  | PARTIAL | FINGER DISLOCATION                                                                | TRAUMA      | 1603       | 6.33       | 30.43  |
| 4  | WORST CASE | TREATED | VISUAL IMPAIRMENT AND/OR INCREASED INTRACRANIAL PRESSURE (VIIP)(SPACE ADAPTATION) | MEDICAL     | 1022       | 4.03       | 34.47  |
| 5  | WORST CASE | PARTIAL | EYE CHEMICAL BURN                                                                 | ENVIRONMENT | 925        | 3.65       | 38.12  |
| 6  | WORST CASE | PARTIAL | NEPHROLITHIASIS                                                                   | MEDICAL     | 811        | 3.20       | 41.32  |
| 7  | WORST CASE | TREATED | NEPHROLITHIASIS                                                                   | MEDICAL     | 689        | 2.72       | 44.04  |
| 8  | WORST CASE | TREATED | SMOKE INHALATION                                                                  | ENVIRONMENT | 674        | 2.66       | 46.70  |
| 9  | WORST CASE | PARTIAL | EYE INFECTION                                                                     | MEDICAL     | 659        | 2.60       | 49.30  |
| 10 | WORST CASE | PARTIAL | DENTAL ABSCESS                                                                    | MEDICAL     | 482        | 1.90       | 51.21  |

**Figure 3: Need for Evacuation (EVAC) – Medical, All DRMs***Error bars are the 95% confidence interval.***Figure 4: Need for Evacuation (EVAC) – Trauma, All DRMs***Error bars are the 95% confidence interval.***Loss of Crew Life (LOCL) Results**

Figure 5 shows the probability of one or more LOCL for all DRMs. LOCL probabilities remain low across shorter missions and increase slightly for the 913-day missions across all crew configurations.

**Figure 5: Loss of Crew Life (LOCL), All DRMs***Error bars are the 95% confidence interval.***Table 9. LOCL Probability, All DRMs**

| DRM / Mission Profile   | Treatment Scenario | LOCL Probability | 95% CI Lower | 95% CI Upper |
|-------------------------|--------------------|------------------|--------------|--------------|
| DRM 1 (42d, Mixed Sex)  | MedCap             | 0.0007           | 0.0006       | 0.0009       |
| DRM 1 (42d, Mixed Sex)  | Treated            | 0.0007           | 0.0006       | 0.0009       |
| DRM 1 (42d, Mixed Sex)  | Untreated          | 0.0030           | 0.0027       | 0.0034       |
| DRM 2 (182d, Mixed Sex) | MedCap             | 0.0033           | 0.0030       | 0.0037       |
| DRM 2 (182d, Mixed Sex) | Treated            | 0.0033           | 0.0029       | 0.0036       |
| DRM 2 (182d, Mixed Sex) | Untreated          | 0.0134           | 0.0128       | 0.0141       |
| DRM 3 (913d, Mixed Sex) | MedCap             | 0.0165           | 0.0156       | 0.0172       |
| DRM 3 (913d, Mixed Sex) | Treated            | 0.0159           | 0.0152       | 0.0167       |
| DRM 3 (913d, Mixed Sex) | Untreated          | 0.0467           | 0.0453       | 0.0480       |
| DRM 4 (42d, All Female) | MedCap             | 0.0007           | 0.0006       | 0.0009       |
| DRM 4 (42d, All Female) | Treated            | 0.0007           | 0.0006       | 0.0009       |
| DRM 4 (42d, All Female) | Untreated          | 0.0035           | 0.0031       | 0.0039       |

| DRM / Mission Profile    | Treatment Scenario | LOCL Probability | 95% CI Lower | 95% CI Upper |
|--------------------------|--------------------|------------------|--------------|--------------|
| DRM 5 (182d, All Female) | MedCap             | 0.0029           | 0.0023       | 0.0033       |
| DRM 5 (182d, All Female) | Treated            | 0.0029           | 0.0026       | 0.0033       |
| DRM 5 (182d, All Female) | Untreated          | 0.0125           | 0.0118       | 0.0131       |
| DRM 6 (913d, All Female) | MedCap             | 0.0157           | 0.0149       | 0.0164       |
| DRM 6 (913d, All Female) | Treated            | 0.0153           | 0.0145       | 0.0160       |
| DRM 6 (913d, All Female) | Untreated          | 0.0456           | 0.0443       | 0.0470       |
| DRM 7 (42d, All Male)    | MedCap             | 0.0008           | 0.0006       | 0.0009       |
| DRM 7 (42d, All Male)    | Treated            | 0.0008           | 0.0006       | 0.0010       |
| DRM 7 (42d, All Male)    | Untreated          | 0.0035           | 0.0031       | 0.0038       |
| DRM 8 (182d, All Male)   | MedCap             | 0.0036           | 0.0032       | 0.0040       |
| DRM 8 (182d, All Male)   | Treated            | 0.0036           | 0.0032       | 0.0039       |
| DRM 8 (182d, All Male)   | Untreated          | 0.0141           | 0.0134       | 0.0148       |
| DRM 9 (913d, All Male)   | MedCap             | 0.0166           | 0.0158       | 0.0174       |
| DRM 9 (913d, All Male)   | Treated            | 0.0161           | 0.0153       | 0.0169       |
| DRM 9 (913d, All Male)   | Untreated          | 0.0508           | 0.0495       | 0.0521       |

## References

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- [1] Integrated Medical Model Project. Integrated Medical Model Operations Plan. JSC-66114. 2011. Houston, TX, NASA, Johnson Space Center. Ref Type: Report
- [2] Integrated Medical Model Project. Integrated Medical Model Software Requirements Specification. IMM-SFTWR-008. 2017. Houston, Texas, KBRwyle Integrated Science, Technology and Engineering. Ref Type: Report
- [3] Integrated Medical Model Project. Integrated Medical Model version 4 Assumptions and Limitations. IMM-GEN-300. 2017. Houston, Texas, KBRwyle Integrated Science and Engineering Space Medicine Information Technology. Ref Type: Report
- [4] NASA-STD-7009: Standard for Models and Simulations (2008). NASA: Washington, DC.
- [5] ISS Medical Checklist (Med CL), 04 June 2014, NASA Johnson Space Center, Medical Operations Group.

## Appendix A: IMM Status at Time of Service Request Report

Validation status for IMM: IMM V&V Matrix shows full MATLAB validation status for each IMM element.

### Compliance with NASA-Standard-7009 Requirements

| Compliance Category   | Number of Requirements |
|-----------------------|------------------------|
| Compliant             | 36                     |
| Compliance Incomplete | 5                      |
| Not Applicable        | 5                      |

### Current NASA-Standard-7009 Credibility Assessment Score (CAS)

| Factor                    | Sufficiency Threshold | Factor Score | Weighted Score |
|---------------------------|-----------------------|--------------|----------------|
| Verification              | 4                     | 3.7          | 0.28           |
| Validation                | 3                     | 3.0          | 0.45           |
| Input Pedigree            | 3                     | 3.0          | 0.53           |
| Results Uncertainty       | 3                     | 3.0          | 0.60           |
| Results Robustness        | 3                     | 3.0          | 0.45           |
| Use History               | 3                     | 3.0          | 0.45           |
| M&S Management            | 2                     | 2.0          | 0.10           |
| People Qualification      | 4                     | 4.0          | 0.20           |
| Overall Credibility Score | -                     | -            | 3.06           |

### Model & Database Metadata

| Item                                        | Details                                         |
|---------------------------------------------|-------------------------------------------------|
| Additional V&V Information                  | None                                            |
| Integrated Medical Evidence Database (iMED) | iMED Lockdown ID: (26), created on (02/21/2017) |
| IMM Version & Platform                      | IMM v4.1 with release 2016a of MATLAB software  |
| Modifications to Code                       | None                                            |

## Appendix B: Medical Conditions in iMED by Category (iMED\_20170221)

The following table details all 100 medical conditions included in the iMED database categorized by type.

### Environmental Conditions (9)

| Condition Name                          |
|-----------------------------------------|
| Acute Radiation Syndrome                |
| Altitude Sickness                       |
| Barotrauma (ear/sinus block)            |
| Burns secondary to Fire                 |
| Decompression Sickness Secondary to EVA |
| Eye Chemical Burn                       |
| Headache (CO2 induced)                  |
| Smoke Inhalation                        |
| Toxic Exposure: Ammonia                 |

### Injury / Trauma Conditions (28)

| Condition Name (Col 1)          | Condition Name (Col 2)                   |
|---------------------------------|------------------------------------------|
| Abdominal Injury                | Acute Compartment Syndrome               |
| Ankle Sprain/Strain             | Back Sprain/Strain                       |
| Chest Injury                    | Dental: Avulsion (tooth loss)            |
| Elbow Dislocation               | Elbow Sprain/Strain                      |
| Eye Irritation/Abrasion         | Eye Penetration (foreign body)           |
| Finger Dislocation              | Fingernail Delamination Secondary to EVA |
| Head Injury                     | Hip Sprain/Strain                        |
| Hip/Proximal Femur Fracture     | Knee Sprain/Strain                       |
| Lower Extremity Stress Fracture | Lumbar Spine Fracture                    |

| Condition Name (Col 1)        | Condition Name (Col 2)             |
|-------------------------------|------------------------------------|
| Neck Sprain/Strain            | Neurogenic Shock                   |
| Paresthesias Secondary to EVA | Shoulder Dislocation               |
| Shoulder Sprain/Strain        | Skin Abrasion                      |
| Skin Laceration               | <b>Traumatic Hypovolemic Shock</b> |
| Wrist Fracture                | Wrist Sprain/Strain                |

### Medical Illness Conditions (63)

| Condition Name (Col 1)                | Condition Name (Col 2)                               |
|---------------------------------------|------------------------------------------------------|
| Abdominal Wall Hernia                 | Abnormal Uterine Bleeding                            |
| Acute Angle-Closure Glaucoma          | Acute Arthritis                                      |
| Acute Cholecystitis/Biliary Colic     | Acute Diverticulitis                                 |
| Acute Pancreatitis                    | Acute Prostatitis                                    |
| Acute Sinusitis                       | Allergic Reaction (mild to moderate)                 |
| Anaphylaxis                           | Angina/Myocardial Infarction                         |
| Anxiety                               | Appendicitis                                         |
| Atrial Fibrillation/Atrial Flutter    | Back Pain (space adaptation)                         |
| Behavioral Emergency                  | Cardiogenic Shock Secondary to Myocardial infarction |
| Choking/Obstructed Airway             | Constipation (space adaptation)                      |
| Dental: Exposed Pulp                  | Dental Caries                                        |
| Dental: Abscess                       | Dental: Crown Loss                                   |
| Dental: Filling Loss                  | Depression                                           |
| Diarrhea                              | Eye Corneal Ulcer                                    |
| Eye Infection                         | Gastroenteritis                                      |
| Headache (Late)                       | Headache (space adaptation)                          |
| Hearing Loss                          | Hemorrhoids                                          |
| Herpes Zoster Reactivation (shingles) | Hypertension                                         |
| Indigestion                           | Influenza                                            |

| Condition Name (Col 1)                                                          | Condition Name (Col 2)                   |
|---------------------------------------------------------------------------------|------------------------------------------|
| Insomnia (space adaptation)                                                     | Medication Overdose/Adverse Reaction     |
| Mouth Ulcer                                                                     | Nasal Congestion (space adaptation)      |
| Nephrolithiasis                                                                 | Nose bleed (space adaptation)            |
| Otitis Externa                                                                  | Otitis Media                             |
| Pharyngitis                                                                     | Respiratory Infection                    |
| Retinal Detachment                                                              | Seizures                                 |
| Sepsis                                                                          | Skin Infection                           |
| Skin Rash                                                                       | Sleep Disorder                           |
| Small Bowel Obstruction                                                         | Space Motion Sickness (space adaptation) |
| Stroke (Cerebrovascular Accident)                                               | Sudden Cardiac Arrest                    |
| Urinary Incontinence (space adaption)                                           | Urinary Retention (space adaptation)     |
| Urinary Tract Infection                                                         | Vaginal Yeast Infection                  |
| Visual Impairment and Increased Intracranial Pressure (VIIP) (space adaptation) |                                          |