Medical Updates to the International Space Station Probabilistic Risk Assessment Model Using the Integrated Medical Model

Presenters:
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Dr. Eric Kerstman, Clinical Lead

Presentation to the Multilateral Medical Operations Panel
NASA Johnson Space Center
SLSD/SD/SD4/Wyle
Houston, TX
4 May 2011
Purpose/Agenda

- **Purpose:** To inform the MMOP of the current IMM capability, and present the updated medical risk estimates approved for use by the Space Station Program.

- **Select the appropriate box below:**
  - [ ] Request for Technical Concurrence
  - [ ] Request for Partial Implementation
  - [ ] Request for Full/Final Implementation
  - **Information Only/Management Direction**
  - [ ] Response to an Action Item

This presentation was previously reviewed/dispositioned at:

<table>
<thead>
<tr>
<th>Meeting</th>
<th>Date</th>
<th>Outcome/Direction</th>
</tr>
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<tr>
<td>Space Medicine CCB</td>
<td>May 2010</td>
<td>Approved. Present to FACB</td>
</tr>
<tr>
<td>Flight Activities Control Board</td>
<td>June 2010</td>
<td>Present to NASA HQ/HMTA</td>
</tr>
<tr>
<td>Health &amp; Medical Technical Authority</td>
<td>June 2010</td>
<td>Approved</td>
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<tr>
<td>Safety &amp; Mission Assurance CCB</td>
<td>Dec 2010</td>
<td>Present to SSPCB</td>
</tr>
<tr>
<td>Space Station Control Board</td>
<td>Dec 2010</td>
<td>Approved. Present to MMOP</td>
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</table>
What is the likelihood of a medical evacuation?

What is the risk of Loss of Crew Life due to illness on ISS?

What medical devices should we have on ISS?

What should be in the Expedition Medical Kit?

Clinical Outcomes and Mission Impact

ISS Medical System Resources

Mission Duration and Profile

Crew Member Attributes

Risks due to EVAs

Medical Condition Incidence Data

Functional Impairments

Medical Resource Attributes

Diagnosis and Treatment of Medical Conditions

Flight Surgeon
Life Now with IMM

Mission Specific Inputs
- Crew Member Attributes
- Crew Composition
- Mission Duration and Profile

Monte Carlo Simulations
- Integrated Medical Model
  - 13,500+ data elements

Quantified Outputs
- Type and Quantity of all medical events
- Risk of EVAC
- Risk of Loss of Crew
- Medical Resources Used
- Optimized medical system within vehicle constraints

Informed Analysis
- Flight Surgeon

ISS Medical System Resources
- Diagnosis and Treatment of Medical Conditions
- Medical Condition Incidence Data
- Risks due to EVAs

IMM Relational Database
Background

• IMM Approach
  • Represents specific (83) medical conditions (including nine space adaptation conditions)
  • Accounts for ISS-based medical capability
  • Bounds clinical outcome uncertainty via best-case, worst-case, and untreated-case scenarios

• IMM development started in June 2005, and funded by Human Research Program

• Transitioned from research to ops, Feb 2011

• Provides evidence-based optimization of in-flight medical system mass and volume
Release History

- FY 2005  Project Kickoff
- April 2008  Project Technical Review
- Sept 2008  IMM v1.0 – Proof of Concept Complete
- Oct 2008  Conceptual Model Review
- Mar 2009  Software Transition from Crystal Ball to SAS 9.1
- Sept 2009  IMM v2.0 – Beta version of relational database
- Oct 2010  IMM v3.0 - Integrated with Database
- Dec 2010  ISS Program Accepts Risk Forecasts
- Feb 2011  Transition to Operational Tool
IMM Evidence Base

- Astronaut Health Database
- ISS Expeditions 1 thru 13 (2006)
- STS-01 thru STS-114 (2005)
- Apollo, Skylab, Mir (U.S. crew only)
- Analog, terrestrial data
- Review of crew medical charts
- Flight Surgeon Subject Matter Expertise
- Russian medical data not used
Comparison – 5x5 Risk Matrix vs. IMM

<table>
<thead>
<tr>
<th>5x5 Matrix</th>
<th>IMM</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Qualitative</td>
<td>• Quantitative</td>
</tr>
<tr>
<td>• Categorical</td>
<td>• Probabilistic, Stochastic</td>
</tr>
<tr>
<td>• Subjective</td>
<td>• Evidence-based</td>
</tr>
<tr>
<td>• Single Risk</td>
<td>• Integrated Risks</td>
</tr>
<tr>
<td>• No Uncertainty</td>
<td>• Uncertainty</td>
</tr>
<tr>
<td>• No Confidence Interval</td>
<td>• Confidence Interval</td>
</tr>
<tr>
<td>• Limited context</td>
<td>• In context</td>
</tr>
</tbody>
</table>

- Medical Conditions & Incidence Data
- Crew Profile
- Mission Profile & Constraints
- Potential crew impairments and mission end states
- In-flight Medical Resources

- Type and quantity of all medical events
- Crew Impairment, Mission and Clinical End States
- Resources used
- Optimized medical system within vehicle constraints
Event Sequence Diagram

Best-case resources available?

Yes → Treated case: Decrement medical resources

No → Untreated Best-Case

Calculate End States:
- Risk of Evacuation
- Risk of Loss of Crew Life
- Type and Quantity of Medical Events organized by Medical, Injury, or Environmental categories
- Crew Functional Impairment
- Resource Utilization and Depletion

Worst-case Scenario

Medical Event

Treated case: Decrement medical resources

No → Untreated Worst-Case

Yes → Untreated Best-Case

Worst-case resources available?
Status of IMM

- Past Uses of the IMM
  - ISS medical system re-design
  - IV Fluid “What if” Assessment
  - Storage Capacity Requirements of Vomitus/Diarrhea for Constellation
  - Constellation medical kit design support
  - ISS Emergency Return Vehicle Analysis
  - Near Earth Asteroid Mission Support (HEFT DRM4)

- Validation and Verification of clinical data
- Documentation of methods and innovations
- Migrating clinical evidence to IMM database
- Establishing web-based external review capability
- Enhancing database reporting capabilities
Verification & Validation (V&V) Status

- Established and implemented V&V Plan
- V&V Plan includes internal and external reviews
- Key IMM elements identified for V&V
- V&V Plan approved via the NASA STD 7009 process
- Established NASA STD 7009 Credibility and Compliance Matrixes for IMM
## Verification & Validation (V&V) Status

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>IMM medical conditions list</td>
<td>✓</td>
<td>✓ a) panel</td>
<td>Pending</td>
</tr>
<tr>
<td>Internal Clinical V&amp;V process</td>
<td>✓</td>
<td>✓ (non-NASA)</td>
<td></td>
</tr>
<tr>
<td>Clinical Inputs (incidence, health impairment, mitigation, consequences, etc.)</td>
<td>30%</td>
<td>Pending (Selected Medical Conditions)</td>
<td>Pending (Selected Medical Conditions)</td>
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<tr>
<td>Model programming</td>
<td>✓</td>
<td>Pending (non-NASA)</td>
<td></td>
</tr>
<tr>
<td>Software and code documentation</td>
<td>✓</td>
<td>Pending (non-NASA)</td>
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</tr>
<tr>
<td>IMM database process</td>
<td>✓</td>
<td>✓ (non-NASA)</td>
<td></td>
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<tr>
<td>IMM output components</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>IMM overall approach</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>IMM output results</td>
<td>✓</td>
<td>✓ a) panel</td>
<td>b) individual SMEs</td>
</tr>
</tbody>
</table>
Methods

- Reference Mission (as defined by ISS PRA Group)
  - 6-person crew (1 female, 5 males)
  - 6-month mission
  - 3 EVAs total for mission
- Industry standard statistical software, SAS 9.1
- Monte Carlo simulations (100K trials)
- Fully-treated scenario using the ISS medical system
Key Assumptions and Limitations

• Accurate diagnosis of all medical events
• Treatments are effective
• 100% reliable medical equipment
• All medical events occur on day one of mission
IMM Definition of Medical Evacuation

• Evacuation is considered as the mission end state when the medical event has the potential to result in any of the following:
  • Loss of crew life
  • Permanent impairment
  • Intractable pain or suffering
  • Inability to complete mission critical tasks
  • Persistent disturbance of behavior, thought or mood that may lead to harm to self or others (psychiatric emergency)
## Results – EVAC and LOC

### ISS Reference Mission - Fully Treated

<table>
<thead>
<tr>
<th>Category</th>
<th>EVAC</th>
<th>EVAC (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Illness</td>
<td>1 in 32</td>
<td>3.14</td>
<td>2.97-3.32</td>
</tr>
<tr>
<td>Injury/Trauma</td>
<td>1 in 169</td>
<td>0.59</td>
<td>0.52-0.67</td>
</tr>
<tr>
<td>Environmental</td>
<td>1 in 135</td>
<td>0.74</td>
<td>0.65-0.81</td>
</tr>
<tr>
<td><strong>All Conditions</strong></td>
<td><strong>1 in 23</strong></td>
<td><strong>4.43</strong></td>
<td><strong>4.25-4.61</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Category</th>
<th>LOC</th>
<th>LOC (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Illness</td>
<td>1 in 270</td>
<td>0.37</td>
<td>0.31-0.43</td>
</tr>
<tr>
<td>Injury/Trauma</td>
<td>1 in 769</td>
<td>0.13</td>
<td>0.10-0.16</td>
</tr>
<tr>
<td>Environmental</td>
<td>1 in 172</td>
<td>0.58</td>
<td>0.49-0.65</td>
</tr>
<tr>
<td><strong>All Conditions</strong></td>
<td><strong>1 in 94</strong></td>
<td><strong>1.06</strong></td>
<td><strong>0.97-1.16</strong></td>
</tr>
</tbody>
</table>
Conversion of % EVAC to events/person-yr

- IMM forecasts a 4.43% probability of EVAC for a 6 crew/6 month ISS mission
  - 6 crew x 0.5 years (6 months) = 3 person-yrs
  - 0.0443 events/3 person-yrs = 0.015 events/person-yr

- IMM forecasts a 1.06% probability of LOC for a 6 crew/6 month ISS mission
  - 6 crew x 0.5 years (6 months) = 3 person-yrs
  - 0.0106 events/3 person-yrs = 0.0035 events/person-yr
Comparison of *Risk of EVAC* Rates

**IMM forecasted Risk of EVAC rate (0.015) compares favorably with literature review EVAC rates (0.010 to 0.072)**

<table>
<thead>
<tr>
<th>Source</th>
<th>Low (events/person-yr)</th>
<th>Max (events/person-yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMM (mean)</td>
<td>0.015</td>
<td>-</td>
</tr>
<tr>
<td>ISS PRA (mean)</td>
<td>0.001</td>
<td>-</td>
</tr>
<tr>
<td>ISS Independent Safety Task Force (February 2007)</td>
<td>0.028</td>
<td>0.042</td>
</tr>
<tr>
<td>Terrestrial General Population</td>
<td>0.060</td>
<td>-</td>
</tr>
<tr>
<td>Antarctic Population</td>
<td>0.036</td>
<td>-</td>
</tr>
<tr>
<td>U.S. Submarine Population</td>
<td>0.023</td>
<td>0.028</td>
</tr>
<tr>
<td>Russian Historical Space Flight Data</td>
<td>0.032</td>
<td>0.072</td>
</tr>
<tr>
<td>LSAH (Astronaut Health) Data</td>
<td>0.010</td>
<td>0.020</td>
</tr>
<tr>
<td>SSF Clinical Experts Seminar Proceedings (1990)</td>
<td>0.010</td>
<td>0.030</td>
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</table>
Validation - Risk of EVAC

**IMM Simulation Data**

Medical illness (71%)
1. Dental Abscess
2. Sepsis
3. Kidney Stones
4. Stroke
5. Atrial Fibrillation
6. Acute Chest Pain/Angina

Injury/Trauma (13%)
1. Hypovolemic Shock
2. Wrist Fracture

Environmental (16%)
1. Smoke Inhalation
2. Toxic Exposure

**Actual Russian Flight Data**

Three EVACs
1. Urosepsis
2. Cardiac Arrhythmia
3. Smoke Inhalation

Three Close Call EVACs
1. Kidney Stone
2. Dental Abscess
3. Toxic Exposure

NOTE: No Russian data are in IMM
Recent Medical Events

- Although papilledema and ocular issues have come to the forefront, currently there is not enough knowledge to know when or if this problem could reach the level requiring evacuation. As data becomes available, it will be added to the model.
Validation – *Risk of LOC* forecast

IMM forecasted *Risk of LOC* rate (0.0035) compares favorably with literature review results for LOC rates (0.0028 to 0.0081)

<table>
<thead>
<tr>
<th>Source</th>
<th>LOC (events/person-yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMM (6 crew/6-month mission)</td>
<td>0.0035</td>
</tr>
<tr>
<td>ISS PRA (3 crew/6-month mission)</td>
<td>0.0006</td>
</tr>
</tbody>
</table>

- **Terrestrial Mortality Rate**
  - 48-year old male: 0.0047 (2006)
  - 48-year old female: 0.0028 (2006)

- **Antarctic**
  - 0.0054 (1904-1964)

- **LSAH Data**
  - 0.0034 (1980-2009)
Validation – ISS Medical Event Estimates

Spider plot comparing the observed (historical data) and expected (model data) number of medical events by mission – ISS (Source: IMM Validation - Goodness of Fit Report for ISS and Shuttle Missions, JSC #TBA)
Validation – Shuttle Medical Event Forecasts

Spider plot comparing the observed (historical data) and expected (model data) number of medical events by mission – Shuttle (Source: IMM Validation - Goodness of Fit Testing for ISS and Shuttle Missions, JSC #TBA)
## Summary of Validation

### Risk of Evacuation (EVAC) Estimates

<table>
<thead>
<tr>
<th>Source</th>
<th>Low (events/person-year)</th>
<th>Max (events/person-year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMM (mean)</td>
<td>0.015</td>
<td>-</td>
</tr>
<tr>
<td>ISS PRA (mean)</td>
<td>0.001</td>
<td>-</td>
</tr>
<tr>
<td>Evidence-based Literature</td>
<td>0.010</td>
<td>0.072</td>
</tr>
</tbody>
</table>

### Risk of Loss of Crew Life (LOC) Estimates

<table>
<thead>
<tr>
<th>Source</th>
<th>Low (events/person-year)</th>
<th>Max (events/person-year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMM (mean)</td>
<td>0.0035</td>
<td>-</td>
</tr>
<tr>
<td>ISS PRA (mean)</td>
<td>0.0006</td>
<td>-</td>
</tr>
<tr>
<td>Evidence-based Literature</td>
<td>0.0028</td>
<td>0.0081</td>
</tr>
</tbody>
</table>
## Comparison of Data – IMM vs. ISS PRA

<table>
<thead>
<tr>
<th>Source Model</th>
<th>Risk of EVAC*</th>
<th>Risk of LOC*</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMM (mean)</td>
<td>0.015 (4.43%)</td>
<td>0.0035 (1.06%)</td>
</tr>
<tr>
<td>ISS PRA (mean)</td>
<td>0.001 (0.35%)</td>
<td>0.0006 (0.17%)</td>
</tr>
<tr>
<td>Difference</td>
<td>x15 factor</td>
<td>x5.8 factor</td>
</tr>
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</table>

* Shown as events/person-year, and percent during mission
Impact to ISS PRA

PRA 2.1.1

PRA 2.1.1 with IMM

EVAC

LOC

EVAC

LOC

1.22E-02 (1 in 82)

8.83E-03 (1 in 113)

5.22E-02 (1 in 19)

1.78E-02 (1 in 56)

1.84E-03 (1 in 544)
Impact to ISS PRA - EVAC

EVAC PRA 2.1.1

EVAC PRA 2.1.1 with IMM
Impact to ISS PRA - LOC

LOC PRA 2.1.1

LOC PRA 2.1.1 with IMM
Forecast of Medical Evacuations on ISS To Date

- 61% probability of no medical evacuation to date
- 39% probability of one or more medical evacuations to date
- Assumes a 4.43% probability of evacuation for a 6-crew, 6-month increment.
  - 3 person-years per increment
- Assumes 33 person-years of ISS crew time to date.
• Medical events will be lead contributor to “Risk of EVAC/LOC”, surpassing ISS PRA estimates of “Risk of EVAC/LOC” from MMOD

• A comprehensive evidence review forms the basis for updating the ISS PRA Risk Model
Open Discussion and Questions
Back-Up Slides
# Updated ISS PRA EVAC and LOC Forecasts

## Probabilities at least one EVAC or LOC

<table>
<thead>
<tr>
<th>Timeframe</th>
<th>Med EVAC Probability</th>
<th>Total EVAC Probability</th>
<th>Med LOC Probability</th>
<th>Total LOC Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISS to Date</td>
<td>39%</td>
<td>44%</td>
<td>11%</td>
<td>18%</td>
</tr>
<tr>
<td>ISS to 2020</td>
<td>74%</td>
<td>79%</td>
<td>27%</td>
<td>42%</td>
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</tbody>
</table>
Emergent Evacuation

IMM Results from Emergency Return Vehicle Trade Study (May 2010)

Estimated Emergent EVAC Probability = 1.2%

1. Kidney Stone                  0.33%
2. Smoke Inhalation            0.22%
3. Toxic Exposure               0.20%
4. Sepsis                             0.15%
5. Hypovolemic Shock        0.10%

Note: Based on 3 crew/6 month ISS mission
Environmental Risk Discussion

- Environmental Conditions in IMM
  - **Smoke Inhalation**
  - **Toxic Exposure**
  - Acute Radiation Syndrome
  - Altitude Sickness
  - Barotrauma (ear/sinus block)
  - Burns
  - Decompression Sickness (EVA)
  - Headache (CO$_2$ induced)
Environmental Risk Discussion

• Differences between ISS PRA and IMM
  • IMM estimates the incidence of smoke inhalation and toxic exposure based on historical data of crew medical events
  • ISS PRA estimates the incidence of smoke inhalation and toxic exposure based on the probability of ISS system failures
  • Since the ISS PRA does not consider the medical risk of smoke inhalation and toxic exposure, it is valid to include these conditions in the IMM as contributors to the risk of EVAC and LOC
### IMM Intravenous Fluids (IV) Analysis

<table>
<thead>
<tr>
<th>Outcome</th>
<th>IV Fluids</th>
<th>No IV Fluids</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHI (%)</td>
<td>93.79</td>
<td>93.48</td>
</tr>
<tr>
<td>EVAC (%)</td>
<td>3.64</td>
<td>7.26</td>
</tr>
<tr>
<td>LOCL (%)</td>
<td>1.09</td>
<td>2.40</td>
</tr>
</tbody>
</table>

Outcomes are based on a 6 month/6 crew ISS mission

※ Conservative (high) estimates of outcomes based on IMM limitation that medical conditions requiring IV fluids go untreated
Validation of Dental Evacuation

<table>
<thead>
<tr>
<th>Outcome</th>
<th>IMM</th>
<th>Military</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dental Evacuation (events/person-yr)</td>
<td>0.006</td>
<td>0.017</td>
</tr>
</tbody>
</table>

References


## Medical Conditions in IMM by Category

<table>
<thead>
<tr>
<th>Medical Illness</th>
<th>Dental Tooth Loss</th>
<th>Nosebleed (SAS)</th>
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</thead>
<tbody>
<tr>
<td>Acute Chest Pain/Angina</td>
<td>Depression</td>
<td>Otitis Externa</td>
</tr>
<tr>
<td>Acute Prostatitis</td>
<td>Diarrhea</td>
<td>Otitis Media</td>
</tr>
<tr>
<td>Allergic Reaction</td>
<td>Eye Abrasion</td>
<td>Pharyngitis</td>
</tr>
<tr>
<td>Anaphylaxis</td>
<td>Eye Corneal Ulcer</td>
<td>Seizures</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Eye Infection</td>
<td>Sepsis</td>
</tr>
<tr>
<td>Appendicitis</td>
<td>Gastroenteritis</td>
<td>Sinus Infection</td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>Glaucoma</td>
<td>Skin Infection</td>
</tr>
<tr>
<td>Back Pain (SAS)</td>
<td>Headache (SAS)</td>
<td>Skin Rash</td>
</tr>
<tr>
<td>Behavioral Emergency</td>
<td>Hemorrhoid</td>
<td>Space Motion Sickness (SAS)</td>
</tr>
<tr>
<td>Cardiogenic Shock</td>
<td>Indigestion</td>
<td>Stroke</td>
</tr>
<tr>
<td>Choking (foreign body inhalation)</td>
<td>Insomnia (SAS)</td>
<td>Sudden Cardiac Arrest</td>
</tr>
<tr>
<td>Constipation (SAS)</td>
<td>Kidney Stones</td>
<td>Urinary Incontinence (SAS)</td>
</tr>
<tr>
<td>Cough (URI/Pneumonia)</td>
<td>Late Insomnia</td>
<td>Urinary Retention (SAS)</td>
</tr>
<tr>
<td>Dental Abscess</td>
<td>Medication OD/Misuse</td>
<td>Urinary Tract Infection</td>
</tr>
<tr>
<td>Dental Crown Replacement</td>
<td>Mouth Ulcer/Cold Sore</td>
<td>Vaginal Yeast Infection</td>
</tr>
<tr>
<td>Dental Temporary Filling</td>
<td>Nasal Congestion (SAS)</td>
<td></td>
</tr>
<tr>
<td>Dental Toothache</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Medical Conditions in IMM by Category

### Injury/Trauma
- Abdominal Injury
- Back Injury
- Chest Injury/Pneumothorax
- Eye Abrasion
- Eye Penetration
- Elbow Dislocation
- Finger Dislocation
- Fingernail Delamination (EVA)
- Head Injury (TBI)
- Hip/Proximal Femur Fracture
- Hypovolemic Shock
- Lumbar Spine Fracture
- Neck Injury
- Neurogenic Shock
- Paresthesias/Hot Spots (EVA)
- Shoulder Dislocation
- Skin Abrasion/Laceration
- Sprain/Strain
- Wrist Fracture

### Environmental
- Acute Radiation Sickness
- Altitude Sickness
- Barotrauma (ear/sinus block)
- Burns
- Decompression Sickness (EVA)
- Eye Chemical Burn
- Headache (CO₂ induced)
- Smoke Inhalation
- Toxic Exposure
IMM System Diagram

- IMM Team
  - Management of references, citations, and SME opinion on centralized IMM library; Provides basis for IMM inputs
  - Citation library sent to SharePoint for use in database

- IMM SQL Database
  - IMM pulls data for simulations
  - Management of model input data, e-CiFFs, approval status of data
  - Configuration management of reports, research, memos, and project documents on SharePoint
  - Citations exported and incorporated in clinical data, e-CiFFs
  - Approved IMM Data; PDF files

- IMM SharePoint on MEME Server
  - SD4 customers access project documents, risk forecasts, trace studies, calendar
  - External reviews for verification and validation of clinical data

- Centralized Reference Manager (RefMan) on BAC Server
  - WIKI (under construction)
  - Restricted Access

- Internal Customers
  - All internal customers access approved medical conditions, incidence data, resources, citations, and levels of evidence

- SD4 Customers
  - Provides IMM related information

- Subject Matter Experts