APPENDIX 4-A

SEVERITY GRADING TABLE AND RECURRENCE INTERVAL DEFINITIONS

Type of Infection/ Severity Grade	Grade 1	Grade 2	Grade 3
Bacterial infections	Bacterial focus NOS requiring no more than 14 days of therapy for treatment (e.g urinary tract infection)	Bacteremia (except CoNS) without severe sepsis ***	Bacteremia with deep organ involvement (e.g. with new or worsening pulmonary infiltrates; endocarditis)
	Coag Neg Staph (S. epi), Corynebacterium, or Proprioniobacterium bacteremia	Bacterial focus with persistent signs, symptoms or persistent positive cultures requiring greater than 14 days of therapy	Severe sepsis with bacteremia.
	Cellulitis responding to initial therapy within 14 days	Cellulitis requiring a change in therapy d/t progression Localized or diffuse infections requiring incision with or without drain placement	Fasciitis requiring debridement
		Any pneumonia documented or presumed to be bacterial	Pneumonia requiring intubation
			Brain abscess or meningitis without bacteremia
	C. Difficile toxin positive stool with diarrhea < 1L without abdominal pain (child < 20 mL/kg)	C. Difficile toxin positive stool with diarrhea $\geq$ 1L (child $\geq$ 20 mL/kg) or with abdominal pain	C. Difficile toxin positive stool with toxic dilatation or renal insufficiency with/without diarrhea
Fungal infections	Superficial candida infection (e.g. oral thrush, vaginal candidiasis)	Candida esophagitis (biopsy proven).	Fungemia including Candidemia
		Proven or probable fungal sinusistis confirmed radiologically without orbital, brain or bone involvement.	Proven or probable invasive fungal infections (e.g., Aspergillus, Mucor, Fusarium, Scedosporium).

Type of Infection/ Severity Grade	Grade 1	Grade 2	Grade 3
Fungal infections continued			Disseminated infections (defined as multifocal pneumonia, presence of urinary or blood antigen, and/or CNS involvement) with Histoplasmosis, Blastomycosis, Coccidiomycosis, or Cryptococcus. *Pneumocystis jiroveci* pneumonia (regardless of PaO2 level)
Viral infections	Mucous HSV infection Dermatomal Zoster Asymptomatic CMV viremia untreated or a CMV viremia with viral load decline by at least 2/3 of the baseline value after 2 weeks of therapy EBV reactivation not treated with rituximab Adenoviral conjunctivitis asymptomatic viruria, asymptomatic stool shedding and viremia not requiring treatment Asymptomatic HHV-6 viremia untreated or an HHV-6 viremia with a viral load decline by at least 0.5 log after 2 weeks of therapy BK viremia or viruria with cystitis not requiring intervention	VZV infection with 3 or more dermatomes Clinically active CMV infection (e.g. symptoms, cytopenias) or CMV Viremia not decreasing by at least 2/3 of the baseline value after 2 weeks of therapy EBV reactivation requiring institution of therapy with rituximab Adenoviral upper respiratory infection, viremia, or symptomatic viruria requiring treatment Clinically active HHV-6 infection (e.g. symptoms, cytopenias) or HHV-6 viremia without viral load decline 0.5 log after 2 weeks of therapy BK viremia or viruia with clinical consequence requiring prolonged therapy and/or surgical intervention	Severe VZV infection (coagulopathy or organ involvement) CMV end-organ involvement (pneumonitis, enteritis, retinitis) EBV PTLD Adenovirus with end-organ involvement (except conjunctivitis and upper respiratory tract)

Type of Infection/ Severity Grade	Grade 1	Grade 2	Grade 3
Viral infections continued	Viremia (virus not otherwise specified) not requiring therapy	Enterocolitis with enteric viruses Symptomatic upper tract respiratory virus Any viremia (virus not otherwise specified) requiring therapy	Lower tract respiratory viruses Any viral encephalitis or meningitis
Parasitic infections			CNS or other organ toxoplasmosis Strongyloides hyperinfection
Nonmicrobiologically defined infections	Uncomplicated fever with negative cultures responding within 14 days Clinically documented infection not requiring inpatient management	Pneumonia or bronchopneumonia not requiring mechanical ventilation Typhlitis	Any acute pneumonia requiring mechanical ventilation Severe sepsis*** without an identified organism

*Concomitant or multimicrobial infections are graded according to the grade of the infection with the higher grade of severity.

**Therapy includes both PO and IV formulations

***Severe Sepsis:

Adults:

Hypotension

-A systolic blood pressure of <90 mm Hg or a reduction of >40 mm hg from baseline in the absence of other causes for hypotension

Multiple Organ Dysfunction Syndrome

-2 or more of the following: Renal failure requiring dialysis, respiratory failure requiring bipap or intubation, heart failure requiring pressors, liver failure

Pediatrics:

-Pediatric SIRS definition and suspected or proven infection and cardiovascular dysfunction or ARDS or TWO or MORE other organ dysfunctions

Pediatric SIRS definition:

Two or more of the following, *one of which must be abnormal temperature or leukocyte count*

1) Core temperature >38.5C ***or*** < 36C
2) Tachycardia, otherwise unexplained persistent in absence of external stimulus, chronic drugs or painful stimuli. ***or*** bradycardia, in < 1 year old, otherwise unexplained persistent.
3) Tachypnea or mechanical ventilation for an acute process not related to underlying neuromuscular disease or general anesthesia
4) Leukocytosis or leukopenia for age (not secondary to chemotherapy) or >10% bands

Pediatric organ dysfunction criteria:

Cardiovavascular: despite administration of fluid bolus ≥40 ml/kg in 1 hour:

- Hypotension <5th percentile for age (***or*** per Table 1)
- Pressors at any dose
- Two of the following:
    - Capillary refill > 5 secs
    - Core to peripheral temperature gap > 3^{o}C
    - Urine output < 0.5 mL/kg/hr
    - Unexplained metabolic acidosis (Base deficit > 5.0 mEq/L)
    - Blood lactate > 2 x ULN

Respiratory:

- ARDS ***or***
- Intubated ***or***
- >50% FiO2 to maintain SaO2 > 92%

Neurological:

- Glasgow Coma Score ≤ 11 ***or***
- Acute change in mental status with a decrease in GSC ≥3 pts from abnormal baseline

Renal:

- Serum creatinine ≥ 2 x ULN for age ***or*** 2-fold increase in baseline creatinine

Hepatic:

- Total bilirubin ≥4 mg/dL ***or***
- ALT ≥2 x ULN for age

TABLE 1: FOUR AGE GROUPS RELEVANT TO HCT:

Age	Tachycardia (bpm)	Bradycardia (bpm)	Tachypnea (breaths/min)	Leukocytosis / Leukopenia (WBC)	Hypotension Systolic BP mmHg
1 mo to 1 yr	>180	<90	>34	>17.5 to <5.0	<100
2 yr to 5 yr	>140	NA	>22	>15.5 to <6.0	<94
6 yr to 12 yr	>130	NA	>18	>13.5 to <4.5	<105
13 yr to < 18 yr	>110	NA	>14	>11 to <4.5	<117

Disseminated Infections:

1. Two or more non-contiguous sites with the SAME organism
2. A disseminated infection can occur at any level of severity, but most will be grade 2 or 3.

Recurrence Intervals to Determine Whether an Infection is the Same or New:

1. CMV, HSV, EBV, HHV6: 2 months (< 60 days)
2. VZV, HZV: 2 weeks (< 14 days)
3. Bacterial, non-C. difficile: 1 week (< 7 days)
4. Bacterial, C. difficile: 1 month (< 30 days)
5. Yeast: 2 weeks (< 14 days)
6. Molds: 3 months (< 90 days)
7. Helicobacter: 1 year (< 365 days)
8. Adenovirus, Enterovirus, Influenza, RSV, Parainfluenza, Rhinovirus: 2 weeks (< 14 days)
9. Polyomavirus (BK virus): 2 months (< 60 days)

For infections coded as "Disseminated" per the *Infection Form*, any previous infection with the same organism but different site within the recurrence interval for that organism will be counted as part of the disseminated infection.