

**NIDDK Liver Transplantation Database
MANUAL OF OPERATIONS (MOOP) DEFINITION**

FORM: MC (CMV DISEASE)

Page 1 of 6

<u>Purpose:</u>	To document each episode of CMV infection (whether new, relapse or persistent), the physical and laboratory findings at the time, treatment for the episode, and outcome at 6 weeks.
<u>Person(s) Responsible:</u>	LTD Clinical Coordinator.
<u>Source(s) of Information:</u>	Medical chart, physician(s) caring for the patient, laboratory reports, biopsy reports.
<u>General Instructions:</u>	This form is to be completed for each episode of CMV, whether treated or untreated. The outcome evaluation should be at 6 weeks after onset of the infection; and again at 4 months if the infection was not resolved at 6 weeks. In the case of resolution and relapse within 6 weeks, each episode should be documented separately; i.e. the initial episode should be filled out with the outcome, and the relapse episode(s) documented on separate form(s) whenever there is an occurrence(s).

**NIDDK Liver Transplantation Database
MANUAL OF OPERATIONS (MOOP) DEFINITION**

FORM: MC (CMV DISEASE)

Page 2 of 6

I.1 EPISODE OF CMV INFECTION

Episode can mean occurrence of new CMV infection or a relapse.

- I.1.1 New: if a new CMV infection has occurred since the previous timepoint.
- I.1.2 Relapse: if the person has had a previous CMV infection (and has been documented on a CMV form), treated or untreated, and cultures return to negative, then turn positive again (check with infectious disease team or transplant teams to verify this), whether the infection is treated or not treated. If the relapse occurs within the same time frame as a new onset of CMV, then both episodes should be documented separately on separate MC forms.
- I.1.3 Persistent (prior to this transplant): if the person has a continuing CMV infection from the time prior to this transplant and at the current time the blood and/or urine remain positive for CMV without clearing. Some people do shed CMV in their urine on and off without having a positive blood culture for CMV.
- I.1.4 Persistent (since this transplant): if the person was CMV culture (-) prior to this transplant, and becomes CMV culture (+) at some time since this transplant, and at the current time the blood and/or urine remain positive for CMV without clearing.
- I.1.5 Unresolved at 6 weeks but currently not present: this is the situation in which a CMV infection was not resolved at 6 weeks, and a follow up is being done at 4 months.

Completing Form: Check one category as appropriate. If "relapse" is checked also record the relapse number. If "persistent" is checked, skip the remainder of the form. If "unresolved" is checked, complete VIII. Outcome.

I.2 FROM THE TIME OF FIRST TRANSPLANT WERE ONLY CMV (-) BLOOD PRODUCTS GIVEN?

Check with the appropriate source (eg. blood bank or crossmatch) to see if the patient has received CMV negative blood products (red cells, platelets) since the time of the first transplant. This is most important for CMV negative recipients.

Completing Form: Check "yes" if only CMV (-) blood products have been given since the time of the first transplant; "no", if CMV (-) blood products were not given, or only some CMV(-) blood products were given, and "unk" if unable to obtain information.

I.3 WAS PROPHYLACTIC CMV THERAPY GIVEN WITHIN 30 DAYS AFTER THE MOST RECENT TRANSPLANT?

Prophylactic CMV therapy could include gancyclovir, acyclovir, or immune globulins.

**NIDDK Liver Transplantation Database
MANUAL OF OPERATIONS (MOOP) DEFINITION**

FORM: MC (CMV DISEASE)

Page 3 of 6

Completing Form: Check "yes" if the patient received prophylactic CMV therapy within 30 days after the most recent transplant; and specify the type of therapy in the space provided. Otherwise, check "no".

II.1 DATE OF DIAGNOSIS OF CMV INFECTION

This is the date of blood draw or urine collection for the first positive culture or serology conversion, or the date of biopsy for the first positive histology.

Completing Form: Record the date as month, day and year.

II.2 WHAT TRIGGERED SUSPICION OF CMV INFECTION?

Documentation of the precipitating events or evidence that led to suspicion of CMV infection.

- II.2.1 CMV serology conversion: if CMV IgM turns from negative to positive, or there is a 4-fold increase in IgG from pretransplant baseline.
- II.2.2 Positive culture(s) or positive histology, or both.
- II.2.3 Elevated liver function tests.
- II.2.4 Clinical symptoms such as arthralgia, fever, GI symptoms, pneumonia.

Completing Form: Check all of the appropriate responses and record the date of onset for symptoms and for elevated LFT's; the date of blood draw for the first positive serology conversion, or the date of biopsy for culture and/or histology. If "clinical symptoms" is checked, also check all of the symptoms that apply. If the symptom is not listed, check "other" and specify. If more than one other, record the remainder under "COMMENTS" (section IX), starting with section no. and item no. (e.g. "II.2.4.6 Other:...").

II.3 WAS DIAGNOSIS BASED ON CMV SEROLOGY CONVERSION ALONE?

CMV IgM turns from negative to positive or there is a 4-fold increase in IgG from pre-transplant baseline.

Completing Form: Check "yes" if the diagnosis was based on CMV serology conversion alone. Otherwise check "no".

III. WAS THE PATIENT SYMPTOMATIC DURING THIS EPISODE?

The following list of symptoms may be present at any time during the CMV episode:

- III.1 Arthralgia
- III.2 Fever
- III.3 Jaundice
- III.4 GI symptoms

**NIDDK Liver Transplantation Database
MANUAL OF OPERATIONS (MOOP) DEFINITION**

FORM: MC (CMV DISEASE)

Page 4 of 6

- III.5 Pneumonitis
- III.6 Retinitis

Completing Form: Check whether the patient was symptomatic during this episode. If "yes", check the appropriate symptoms on the list, and the date of onset of each. If "Fever" is checked, also record the duration in days. If the symptom is not listed, check "other" and specify. If there is more than one other, record the remainder under "COMMENTS" (section IX), starting with section number and item number (e.g. "III.8 Other . . .").

IV. SEVERITY INDEX

The severity index is to categorize the status of the patient during the CMV episode. The item checked should reflect the worst status during the episode.

- IV.1 Asymptomatic, outpatient/at home: patient is asymptomatic and never hospitalized for any reason during this CMV episode.
- IV.2 Asymptomatic, hospitalized: patient is asymptomatic for CMV, but hospitalized for some other reason not related to this episode of CMV infection.
- IV.3 Symptomatic, outpatient/at home: patient has symptoms with this CMV episode, but never hospitalized during this CMV episode.
- IV.4 Symptomatic, in hospital/admitted for other reasons: patient has symptoms with this CMV episode, but admitted to hospital for some reason not related to this episode of CMV.
- IV.5 Symptomatic, in hospital/admitted for CMV: patient has symptoms with this CMV episode and has been admitted because of this CMV infection only.
- IV.6 Symptomatic, hospitalized in intensive care unit: patient has symptoms with this CMV episode, and has been admitted to the ICU because of this CMV infection only.

Completing Form: Check the appropriate response to indicate the status of the patient for this episode.

V. BIOCHEMICAL PARAMETERS

These laboratory tests should be done at least once during an episode of CMV infection.

- V.1 Alkaline phosphatase
 - 1. Normal range: varies with each center (recommend 30 to 530 U/L).
 - 2. Edit range: 30 to 5000 U/L.
- V.2 SGPT (ALT)
 - 1. Normal range: varies with each center (recommend 2 to 56 U/L).

**NIDDK Liver Transplantation Database
MANUAL OF OPERATIONS (MOOP) DEFINITION**

FORM: MC (CMV DISEASE)

Page 5 of 6

2. Edit range: 1 to 5,000 U/L.

V.3 GGT

1. Normal range: varies with each center (recommend 6 to 85 U/L).
2. Edit range: 1 to 1,500 U/L.

V.4 Total bilirubin

1. Normal range: 0.0 to 1.2 mg/dl.
2. Edit range: 0.0 to 76.0 mg/dl.

V.5 Platelet count

1. Normal range: 140×10^3 to 451×10^3 cells/mm³.
2. Edit range: 10×10^3 to 600×10^3 cells/mm³.

V.6 WBC

1. Normal range: 3.4×10^3 to 38.0×10^3 cells/mm³.
2. Edit range: 1.0×10^3 to 71.0×10^3 cells/mm³.

Completing Form:

- V.1 Alkaline phosphatase: record the highest value during the CMV infection and record date sample was drawn.
- V.2 ALT: record the highest value during the CMV infection and record date sample was drawn.
- V.3 GGT: record the highest value during the CMV infection and record date sample was drawn.
- V.4 Total bilirubin: record the highest value during the CMV infection and record date sample was drawn.
- V.5 Platelet count: record the lowest value during the CMV infection and record date sample was drawn.
- V.6 WBC: record the lowest value during the CMV infection and record date sample was drawn.

VI. WERE CULTURES/TESTS DONE DURING THIS EPISODE?

Cultures and tests to be documented for this CMV episode include: 1) blood culture for CMV; 2) BAL culture for CMV; 3) CMV serology conversion; 4) urine culture for CMV; tissue biopsies of 5) liver, 6) lung, and 7) GI; and 8) other test. Tests done for these biopsies include CMV culture, inclusion bodies, immunoperoxidase monoclonal, polyclonal, and CMV DNA probing.

Completing Form: Check whether any cultures or tests for CMV were done during this episode. If "yes", check all of the tests that were done and record the results as positive or negative. For each test, if the result was positive, record the date of the sample of the first positive result as month/day/year; if the results were always negative, record the date of the most recent sample. If a culture or test other than the listed was done, check "other" and specify the type. If more than one "other" was done, record the remainder under "COMMENTS" (section IX), starting

**NIDDK Liver Transplantation Database
MANUAL OF OPERATIONS (MOOP) DEFINITION**

FORM: MC (CMV DISEASE)

Page 6 of 6

with section number and item number (e.g. "VI.9 Other . . .").

VII. WAS TREATMENT GIVEN?

Treatment for CMV infection could include gancyclovir, gamma globulin, reduced protocol immunosuppressive medications (such as Imuran or prednisone), or other types of medication.

Completing Form: Check whether any treatment was given. If "yes", check all types of treatment given. Under gancyclovir, record the total daily dosage in mgs. and the dates given. If other type of medication was given for CMV, check "other" and specify. If more than one "other" was given, record the remainder under "COMMENTS" (section IX), starting with section number and item number (e.g. "VII.4 Other . . .").

VIII. OUTCOME

The outcome at a specified time point can be 1) not evaluated, no cultures done; 2) persistent CMV; 3) cure from CMV infection; 4) retransplantation; 5) death from CMV; 6) death from other cause(s). The evaluation date is the date that this evaluation is made, usually at 6 weeks after the onset of the CMV infection. The outcome date is the date of the event (retransplantation or death) or determination of cure.

Completing Form: Record the date of this evaluation as month/day/year. Check one of the following outcomes: 1) not evaluated, no cultures done; 2) persistent CMV - if this is checked, further check whether it is viuria (urine), viremia (blood), or "other" and specify; 3) cure from CMV infection; 4) retransplanted; 5) if the person died because of the CMV infection, or 6) died from causes other than CMV. Also give the date (month/day/year) of cure, retransplant, or death.

IX. COMMENTS

Use this space for any other information that is pertinent to this CMV episode, that has not been recorded elsewhere in this form.

Completing Form: Check whether there are any comments to be made. If "yes" write in the comments that are pertinent to this episode of CMV infection.