

**Actions from Peer Review of the Draft Report on Carcinogens
Monographs on Selected Viruses: Human T-cell Lymphotropic Virus Type 1 [HTLV-1],
Epstein-Barr Virus [EBV], Merkel Cell Polyomavirus [MCV], Kaposi Sarcoma-associated
Herpesvirus [KSHV], and Human Immunodeficiency Virus Type 1 [HIV-Type1]**

December 17, 2015

The NTP Peer-Review Panel (“the Panel”) was convened on December 17, 2015, to peer review draft Report on Carcinogens (RoC) monographs on five viruses: Human T-cell Lymphotropic Virus Type 1 [HTLV-1], Epstein-Barr Virus [EBV], Merkel Cell Polyomavirus [MCV], Kaposi Sarcoma-associated Herpesvirus [KSHV], and Human Immunodeficiency Virus Type 1 [HIV-Type1]. A meeting report will be prepared and posted to the NTP website when completed. The Panel peer reviewed the draft monographs and provided its opinion on the NTP’s draft conclusions for the level of evidence for carcinogenicity from human studies and the NTP’s preliminary listing decision for each of the viruses. NTP will consider the Panel’s peer-review comments in finalizing the monographs. When completed, the monograph will be published on the NTP website (<http://ntp.niehs.nih.gov/go/roc>).

The Panel concurred with the statement that a significant number of persons living in the United States are exposed to each of the five viruses.

HTLV-1

The Panel voted unanimously (6 yes, 0 no, 0 abstentions) to:

- Accept the draft NTP conclusion that the scientific information presented from human cancer studies on HTLV-1 supports the level of evidence conclusion of *sufficient evidence of carcinogenicity* for adult T-cell leukemia/lymphoma
- Recommend the conclusion of *inadequate evidence* of carcinogenicity for liver cancer.

The Panel agreed unanimously (6 yes, 0 no, 0 abstentions) with the NTP’s preliminary policy decision to list HTLV-1 in the RoC as *known to be a human carcinogen* based on sufficient evidence from studies in humans. This conclusion is based on evidence from epidemiological and molecular studies, which shows that HTLV-1 causes adult T-cell leukemia/lymphoma and on supporting mechanistic data.

EBV

The Panel voted unanimously (6 yes, 0 no, 0 abstentions) to:

- Accept the draft NTP conclusion that the scientific information presented from human cancer studies on EBV supports the level of evidence conclusions of (1) *sufficient evidence of carcinogenicity* for Burkitt lymphoma (endemic), Hodgkin lymphoma, nasopharyngeal cancer, immunosuppression-related non-Hodgkin lymphoma, extranodal NK/T-cell lymphoma (nasal type), and gastric cancer and (2) *limited evidence of carcinogenicity* for Burkitt lymphoma (sporadic).

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- Recommend the conclusion of *inadequate evidence of carcinogenicity* for lymphoepithelial cancer of the salivary gland.

The Panel agreed unanimously (6 yes, 0 no, 0 abstentions) with the NTP's preliminary policy decision to list EBV in the RoC as *known to be a human carcinogen* based on sufficient evidence from studies in humans. This conclusion is based on evidence from epidemiological, clinical, and molecular studies, which show that EBV causes endemic Burkitt lymphoma, Hodgkin lymphoma, immune-suppression-related non-Hodgkin lymphoma, extranodal natural killer-T-cell lymphoma (nasal type), nasopharyngeal carcinoma, and some forms of gastric cancer. There is also limited evidence for an association with Burkitt lymphoma (sporadic).

MCV

The Panel voted (5 yes, 1 no, 0 abstentions) that the scientific information presented from human cancer studies on MCV supports the NTP's preliminary level of evidence conclusion of *sufficient evidence of carcinogenicity* for Merkel cell carcinoma.

The Panel voted (5 yes, 1 no, 0 abstentions) that the NTP's preliminary policy decision to list MCV in the RoC as *known to be a human carcinogen* is based on sufficient evidence from studies in humans. This conclusion is based on evidence from epidemiological, clinical, and molecular studies, which show that MCV causes Merkel cell carcinoma, and on supporting mechanistic data.

KSHV

The Panel voted unanimously (6 yes, 0 no, 0 abstentions) to:

- Accept the draft NTP conclusion that the scientific information presented from human cancer studies on KSHV supports the level of evidence conclusion of *sufficient evidence of carcinogenicity* for Kaposi sarcoma and primary effusion lymphoma.
- Recommend the conclusion of *sufficient evidence of carcinogenicity* for multicentric Castleman disease (plasmablastic variant).

The Panel agreed unanimously (6 yes, 0 no, 0 abstentions) with the NTP's preliminary policy decision to list KSHV in the RoC as *known to be a human carcinogen* based on sufficient evidence from studies in humans. This conclusion is based on evidence from epidemiological and molecular studies, which shows that KSHV causes Kaposi sarcoma, primary effusion lymphoma, and multicentric Castleman disease (plasmablastic variant), and on supporting mechanistic data.

HIV-Type 1

The Panel voted unanimously (6 yes, 0 no, 0 abstentions) to:

- Accept the draft NTP conclusion that the scientific information presented from human cancer studies on HIV-Type 1 supports the level of evidence conclusion of *sufficient evidence of carcinogenicity* for Kaposi sarcoma, non-Hodgkin lymphoma, Hodgkin

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lymphoma, invasive anal cancer, genital cancers (vaginal/vulvar and penile), conjunctival cancer, and non-melanoma skin cancer.

The Panel voted (5 yes, 1 no, 0 abstentions) to:

- Accept the draft NTP conclusion that the scientific evidence presented from human cancer studies on HIV-Type 1 supports the level of evidence conclusion of *limited evidence of carcinogenicity* for liver cancer and oral cancer.
- Recommend the conclusion of *limited evidence of carcinogenicity* for invasive cervical cancer.
- Recommend the conclusion of *inadequate evidence of carcinogenicity* for lung cancer.

The Panel concurred with the NTP's preliminary policy decision to list HIV-Type 1 in the RoC as *known to be a human carcinogen* based on sufficient evidence from studies in humans. The Panel voted (5 yes, 1 no, 0 abstentions) that this conclusion is based on epidemiological studies showing that HIV-1 increases the risk of Kaposi sarcoma, non-Hodgkin lymphoma, Hodgkin lymphoma, invasive anal cancer, genital cancers (vaginal/vulvar and penile cancers), conjunctival eye cancer, and non-melanoma skin cancer, together with supporting evidence from mechanistic studies demonstrating the biological plausibility of its carcinogenicity in humans. Epidemiological studies also provide limited evidence for an association between HIV-1 infection and oral cancer, liver cancer, and invasive cervical cancer.