Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States

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Long-Term Follow-Up of Antiretroviral Drug-Exposed Infants (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendations
• Children with *in utero*/neonatal exposure to antiretroviral (ARV) drugs who develop significant organ system abnormalities of unknown etiology, particularly of the nervous system or heart, should be evaluated for potential mitochondrial dysfunction **(CIII)**. • Follow-up of children with exposure to ARVs should continue into adulthood because of the theoretical concerns regarding the potential for carcinogenicity of nucleoside analogue ARV drugs **(CIII)**.
Rating of Recommendations: *A = Strong; B = Moderate; C = Optional* ***Rating of Evidence:*** *I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Data remain insufficient to address the effect that exposure to zidovudine or other antiretroviral (ARV) agents *in utero* might have on long-term risk of neoplasia or organ system toxicities in children. Data from follow-up of PACTG 076 infants through age 6 years do not indicate any differences in immunologic, neurologic, and growth parameters between infants who were exposed to the zidovudine regimen and those who received placebo, and no malignancies have been seen.[1-3] As discussed earlier in NRTI Drugs and Mitochondrial Toxicity, data are conflicting regarding whether mitochondrial dysfunction is associated with perinatal exposure to ARVs. Children with *in utero* exposure to ARVs who develop significant organ system abnormalities of unknown etiology, particularly of the nervous system or heart, should be evaluated for potential mitochondrial dysfunction.[4-6] Follow-up of children with exposure to ARVs should continue into adulthood because of the theoretical concerns regarding the potential for carcinogenicity of the nucleoside analogue ARV drugs. Long-term follow-up should include annual physical examinations of all children exposed to ARV drugs. Innovative methods are needed to provide follow-up of infants with *in utero* exposure to ARV drugs. Information regarding such exposure should be part of ongoing permanent medical records for children, particularly those who are uninfected.

Evaluation is ongoing of early and late effects of *in utero* exposure to ARVs, including the Pediatric HIV/AIDS Cohort Study, Surveillance Monitoring of Antiretroviral Toxicity Study, natural history studies, and HIV/AIDS surveillance conducted by state health departments and the Centers for Disease Control and Prevention. Because most of the available follow-up data relate to *in utero* exposure to antenatal zidovudine alone and most HIV-infected pregnant women currently receive combination ARV drug regimens, it is critical that studies to evaluate potential adverse effects of *in utero* drug exposure continue to be supported. HIV surveillance databases from states that require HIV reporting provide an opportunity to collect population-based information concerning *in utero* exposure to ARVs. To the extent permitted by federal law and regulations, data from these confidential registries can be compared with information from birth defect and cancer registries to identify potential adverse outcomes.

References

1. Culnane M, Fowler M, Lee SS, et al. Lack of long-term effects of *in utero* exposure to zidovudine among uninfected children born to HIV-infected women. Pediatric AIDS Clinical Trials Group Protocol 219/076 Teams. *JAMA*. Jan 13 1999;281(2):151-157. Available at http://www.ncbi.nlm.nih.gov/pubmed/9917118.
2. Hanson IC, Antonelli TA, Sperling RS, et al. Lack of tumors in infants with perinatal HIV-1 exposure and fetal/neonatal exposure to zidovudine. *J Acquir Immune Defic Syndr Hum Retrovirol*. Apr 15 1999;20(5):463-467. Available at

http://www.ncbi.nlm.nih.gov/pubmed/10225228.

3. Brogly S, Williams P, Seage GR, 3rd, Van Dyke R. *In utero* nucleoside reverse transcriptase inhibitor exposure and cancer in HIV-uninfected children: an update from the pediatric AIDS clinical trials group 219 and 219C cohorts. *J Acquir Immune Defic Syndr*. Apr 1 2006;41(4):535-536. Available at http://www.ncbi.nlm.nih.gov/pubmed/16652068.
4. Blanche S, Tardieu M, Rustin P, et al. Persistent mitochondrial dysfunction and perinatal exposure to antiretroviral nucleoside analogues. *Lancet*. Sep 25 1999;354(9184):1084-1089. Available at http://www.ncbi.nlm.nih.gov/pubmed/10509500.
5. Barret B, Tardieu M, Rustin P, et al. Persistent mitochondrial dysfunction in HIV-1-exposed but uninfected infants: clinical screening in a large prospective cohort. *AIDS*. Aug 15 2003;17(12):1769-1785. Available at http://www.ncbi.nlm.nih.gov/pubmed/12891063.
6. Spector SA, Saitoh A. Mitochondrial dysfunction: prevention of HIV-1 mother-to-infant transmission outweighs fear. *AIDS*. Aug 22 2006;20(13):1777-1778. Available at http://www.ncbi.nlm.nih.gov/pubmed/16931943.