

**Scientific Working Group on SAEs in *Loa loa* endemic areas**  
The Shrigley Hall Hotel, Manchester, UK  
**28-30 May 2002**

**Case Definitions of *Loa loa* encephalopathy  
temporally related to treatment with Mectizan®**

**Definite Case of *L. loa* Encephalopathy**

- encephalopathy in which brain tissue obtained by autopsy or by needle sampling has microscopic findings consistent with *L. loa* encephalopathy (vasculopathy with evidence of *L. loa* microfilariae as a likely etiology), and
- onset of Central Nervous System (CNS) symptoms and signs within 7 days of treatment with Mectizan®; illness progressing to coma without remission.

**Probable Case of *L. loa* Encephalopathy**

- encephalopathy (without seizures, usually with fever) in a person previously healthy and has no other underlying cause for encephalopathy, and
- onset of CNS symptoms and signs within 7 days of treatment with Mectizan®; illness progressing to coma without remission, and
- peripheral blood *L. loa* > 10,000 mf/ml pre-treatment, or > 1,000 mf/ml within 2 months post-treatment, or > 2700 mf/ml within 6 months of treatment; and/or *L. loa* microfilariae present in cerebrospinal fluid (CSF).

**Possible Case of *L. loa* Encephalopathy**

- encephalopathy (without seizures, usually with fever) in a person previously healthy and has no other underlying cause for encephalopathy, and
- onset of CNS symptoms and signs within 7 days of treatment with Mectizan®; illness progressing to coma without remission, and
- semi-quantitative or non-quantitative positive (i.e. +, ++, +++) *L. loa* microfilariae in peripheral blood or CSF.

**Encephalopathy of other known etiology**

- encephalopathy with sufficient clinical information to determine an etiology other than *L. loa* (e.g. cerebral malaria)

**Encephalopathy of unknown etiology**

- encephalopathy in a person previously healthy and has no other underlying cause for encephalopathy, and
- onset of CNS symptoms and signs within 7 days of treatment with Mectizan®, and

- laboratory findings are inadequate to determine probable etiology.

These definitions were adapted from those originally put forth in 1995<sup>1</sup>, by an independent group of experts that consulted for the MDP, in the following ways:

- the timeframe within which a case would be considered was extended from 5 to 7 days because a prospective study conducted in 1997 showed that the onset of symptoms may be as late as 7 days post-treatment<sup>2</sup>;
- the thresholds for the quantitative *L. loa* laboratory studies were broadened to include samples taken 5 or 6 months post-treatment since several encephalopathic cases in Cameroon who were treated in peripheral health centers and had no laboratory studies performed initially, were subsequently evaluated in their villages by a team of clinicians sponsored by the national-level Ministry of Health; the threshold for 6 months post-treatment was derived from a calculation based on the finding that on average, *L. loa* microfilarial loads are reduced by at least 73% six months after a single dose of Mectizan® (150\_g/kg)<sup>3</sup>; the pre-treatment threshold of 10,000 mf/ml was assumed to still be valid, thus 73% of 10,000 gave rise to 2,700 mf/ml at 6 months post-treatment;

**the category of 'possible' *L. loa* encephalopathy was added to the list of presumptive diagnoses to better capture the reality of the field situation where most of the encephalopathic cases were treated in peripheral hospitals which were typically not equipped to perform quantitative *L. loa* studies.**

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<sup>1</sup> Anonymous (1996). Central Nervous System (CNS) Complications of Loiasis and Adverse CNS Events following Treatment: Report of an invited consultation, 2-3 October 1995 (Atlanta, GA: Mectizan® Donation Program, 1996).

<sup>2</sup> Gardon J, Gardon-Wendel N, Ngangue D, Kamgno J, Chippaux J-P, Boussinesq M (1997) Serious reactions after mass treatment of onchocerciasis with ivermectin in an area endemic for *Loa loa* infection. *Lancet* **350**, 18-22.

<sup>3</sup> Gardon J, Kamgno J, Folefack G, Gardon-Wendel N, Bouchite B, Boussinesq M (1997) Marked decrease in *Loa loa* microfilaraemia six and twelve months after a single dose of ivermectin. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **91**, 593-594.