30 S. Castle St.
Baltimore, MD 21231

March 5, 2015

Carrie Hessler-Radelet
Director, The Peace Corps
1111 20th St. NW
Washington, DC 20526

Dear Director Hessler-Radelet,

We write in support of a group of returned Peace Corps Volunteers (RPCVs) who took the antimalarial drug mefloquine as part of their service. As former military physicians deeply familiar with the adverse health effects of this drug, we are writing to add our voice to their concerns about current Peace Corps antimalarial policy and to encourage your office to consider a change. A recent description of current policy reads:

> *Volunteers meet individually with their Peace Corps Medical Officer to discuss the risks, benefits and side effects of the malaria suppression medications available to them. Volunteers are then given a choice of medication, depending on their location and whether they prefer a daily or weekly regimen*[1].

In locations with chloroquine-resistant malaria, the medications referred to are doxycycline, atovaquone-proguanil (Malarone), and mefloquine. We are concerned by the implication of current policy that these drugs are still considered equally safe by the Peace Corps and that dosing frequency is the most important difference between them.

These drugs are not equally safe. Only one of these drugs, mefloquine, now carries a boxed warning of potentially permanent neuropsychiatric effects. Only one of these drugs, mefloquine, requires careful monitoring for the development of prodromal symptoms, including anxiety, paranoia, hallucinations, depression, restlessness, unusual behavior or confusion, which may predict the development of permanent neuropsychiatric effects. Only one of these drugs, mefloquine, requires patients prescribed the drug be issued a medication guide and wallet card containing instructions that warn the patient of the need to discontinue the medication at the onset of any of these symptoms[3]. Similarly, only one of these drugs, mefloquine, takes weeks, not days, to build up to protective steady state levels in the blood[4].

We are concerned that current Peace Corps policy does not adequately acknowledge the special requirements that accompany responsible use of this medication. The Centers for Disease Control and Prevention (CDC) notes that mefloquine "needs to be started at least 2 weeks *prior to travel*"[5] (emphasis added), and recommends beginning the drug up to 4 weeks in advance to permit careful assessment of prodromal symptoms:

> *For example, mefloquine can be started 3–4 weeks in advance to allow potential adverse events to occur before travel. If unacceptable side effects develop, there would be time to change the medication before the traveler's departure*[6].

Responsible policy would ensure time for such a trial prior to a volunteer's travel. In contrast, it would be inappropriate policy to delay the dispensing of mefloquine until only after a volunteer has arrived in-country, as this would risk prodromal symptoms being overlooked or misattributed to causes such as the stresses of travel, thus increasing the risk of permanent neuropsychiatric effects should the drug not be discontinued at their onset. Additionally, even if prodromal symptoms do not develop, mefloquine, unlike other drugs, can take up to 7–10 weeks of dosing to build to protective steady state levels in the blood[4]. Responsible policy would ensure time for the drug to adequately build to these desired levels prior to a volunteer's travel. In contrast, it would be inappropriate policy to encourage a volunteer to begin taking a temporary course of doxycycline or Malarone after arrival in-country, while simultaneously beginning mefloquine in anticipation of its later exclusive use once it has reached protective levels. Such a practice again risks prodromal symptoms being overlooked or misattributed to other causes. Additionally, CDC currently does not recommend switching from doxycycline or Malarone to mefloquine while in a malaria-endemic area[6].

Military experience substantiates that the perceived advantages of mefloquine's weekly dosing do not in practice result in improved adherence, nor improved protection from malaria, even during prolonged overseas deployments[7]. Cognizant of this fact, the U.S. Army Special Operations Command, whose members frequently deploy to remote settings comparable to those where Peace Corps volunteers serve, has banned the use of mefloquine altogether[8].

Given mefloquine's lack of advantage, and its very real risks, we believe that the most responsible course of action for the Peace Corps is to discontinue its use altogether, replacing it with safer and better-tolerated alternatives doxycycline and Malarone for volunteers travelling to areas of chloroquine-resistant malaria.

If, however, the Peace Corps determines that mefloquine must continue to be used, we strongly encourage you to swiftly enact the following policy to improve the safety of such use:

> *Peace Corps volunteers who choose mefloquine will be issued a test prescription at least four weeks (and ideally 7 – 10 weeks) prior to travel to allow them to be carefully monitored by medical professionals for the development of prodromal symptoms and to permit the drug to achieve steady state levels. Loading doses of mefloquine (i.e. administering more than one 250mg tablet per week) will not be used. Only after a thorough examination for neuropsychiatric effects will Peace Corps volunteers who appear to tolerate their mefloquine test prescription be issued their full prescription for overseas travel. These volunteers will also be issued a secondary prescription for doxycycline or Malarone, to be used in place of mefloquine as malaria prophylaxis should prodromal symptoms develop during their service. Mefloquine will never be used as a "drug of last resort" if the volunteer cannot tolerate an alternative antimalarial medication, and volunteers will never be switched to mefloquine from another antimalarial drug while in-country. Peace Corps Medical Officers and trainees will receive additional training in the recognition of prodromal symptoms and in the significance of information contained in the mefloquine boxed warning, to include the drug's potential to cause neuropsychiatric effects which may be permanent. Peace Corps volunteers completing any course of mefloquine will be carefully evaluated for the presence of neuropsychiatric effects including those highlighted in the boxed warning, and if present, these will be thoroughly evaluated by medical professionals, and reported by the Peace Corps to the U.S. Food and Drug Administration.*

The group of RPCVs that we represent love the Peace Corps and are proud of their service, but for this group, the adverse health effects of mefloquine are not simply words in a warning box. Having in many cases suffered permanent disability from their use of the drug, they wish to ensure that future Peace Corps volunteers do not suffer the same effects.

Peace Corps volunteers must be kept safe from malaria, but they must be kept safe from malaria in a responsible manner, protected as much as possible from the potentially permanent adverse effects of medicines used inappropriately in its prevention.

We trust that you share these goals, and that you will act on these recommendations to improve Peace Corps antimalarial policy.

Sincerely,

Remington Nevin, MD, MPH
Formerly, MAJ, US Army Medical Corps

Elspeth Cameron Ritchie, MD, MPH
COL (Retired), US Army Medical Corps

CC (by email): Peace Corps Office of Medical Services
CDC Center for Global Health,
Division of Parasitic Diseases and Malaria
RPCVs (list enclosed)

Attachments: References
RPCVs

References

1. Peace Corps. "Ensuring Volunteers' Health During & After Service". July, 2014. Available at: http://files.peacecorps.gov/multimedia/pdf/learn/benefits/health_progress_fact_sheet.pdf

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4. Whitman TJ, Coyne PE, Magill AJ, et al. An outbreak of Plasmodium falciparum malaria in U.S. Marines deployed to Liberia. The American journal of tropical medicine and hygiene 2010;83(2):258-65

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RPCVs

Suzanne Alton
Gabon, 1983-1985

Timothy Coull
Burkina Faso, 2010

Kevin Croft
Benin, 1992-1994

Paddy Daly
Tanzania, 2010

Mary Kay Diakite
Mali, 1996-1998

Christie-Anne Edie
Madagascar, Burkina Faso, 2008-2010

Nicholas Edwards
Mozambique, 2010-2011

Diana Farias
Liberia, 2014

David Fields
Ghana, 2011-2013

Brittany Freitas
Zambia, 2008-2011

Genevieve Gallagher
Togo, 1996-1997

Martin Giannini
Togo, 1995-1997

Tony Giglini
Niger, 1998-1999

Garrison Harward
Senegal, 2010-2012

Christi Haynie
Malawi, 1996-1997

Emily Hooker
Burkina Faso, 2010-2012

Felicia Kenney
Benin, 2003-2004

Yoel Kirschner
Malawi, 2009-2011

Jennifer Mamola
Uganda, 2012-2013

Patrick McClanahan
Mozambique, 2010-2011

Viola McNally
Burkina Faso, 2010

James Megivern
Burkina Faso, 2010-2012

Kenn Miller
Senegal, 2001-2003

Samuel Mills
Lesotho, 2006-2007

Allegra Panetto
Malawi, 2010-2012

Mark Schafer
Malawi, 1989-1991

Ben Siegelman
Malawi, 2010-2012

Marina Spencer
Burkina Faso, 2010-2012

Richard Stoll
APCD, East Timor, 2004-2005

Yorgos Strangas
Malawi, 2009-2011

Adam Stuart
Malawi 2010-2012

Joseph Sullivan
Zambia, 1999-2001

George Swansea
Malawi, 1996-1998

Austin Swift
Burkina Faso, 2010-2012

Kaitlin Thompson
Burkina Faso, 2010-2012

Sara Thompson
Burkina Faso, 2010