DRUG ABUSE

An exploration of the government’s use of mefloquine at Guantanamo

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Executive Summary

Mefloquine is an antimalarial drug that has long been known to cause severe neuropsychological adverse effects such as anxiety, paranoia, hallucinations, aggression, psychotic behavior, mood changes, depression, memory impairment, convulsions, loss of coordination (ataxia), suicidal ideation, and possibly suicide, particularly in patients with a history of mental illness. A prescribing physician must exercise caution and informed judgment when weighing the risks and potential benefits of prescribing the drug. To administer this drug with its severe potential side effects without a malaria diagnosis and without taking a patient’s mental health history is not medically justified. Yet as a matter of official policy, the standard operating procedure implemented by the United States military at Guantanamo Bay was to administer high doses of mefloquine to detainees whether or not any use of the drug was medically appropriate and without consideration of the detainees’ mental health.

It is clear that the military employed a medically inappropriate treatment regime at Guantanamo Bay (GTMO). It is less clear why, although the available evidence supports several possible conclusions. In view of the continued and unexplained refusal of the government to release full medical records for all detainees, it is not possible to determine whether this conduct was gross malpractice or deliberate misuse of the drug. In either case, it does not appear plausible from the available evidence that mefloquine was given to treat malaria. This suggests a darker possibility: that the military gave detainees the drug specifically to bring about the adverse side effects, either as part of enhanced interrogation techniques, experimentation in behavioral modification, or torture for some other purpose. While this Report does not reach a conclusion about the actual motives for this course of conduct, it does explore the legal rules that would apply were it determined that mefloquine was administered not to treat malaria but rather to exploit the neuropsychiatric effects of the drug.
Findings:

This Report demonstrates that the U.S. military routinely administered doses of mefloquine to detainees upon their arrival at GTMO without medical justification:

- 1250 mg of mefloquine was given to all detainees as a standard measure during inprocessing.
- Mefloquine is used for treatment of malaria only in mild to moderate cases of infection with the p. vivax or p. falciparum parasite.
- At GTMO, mefloquine was given to detainees before testing them for malaria, without regard for whether the detainee actually had malaria at all, let alone whether he carried one of the parasites treatable by mefloquine.
- The standard of care rejects administering mefloquine to persons with a history of mental illness or a family history of mental illness, due to a greatly increased risk of severe adverse side effects for such persons.
- At GTMO, mefloquine was given to detainees without regard to prior mental health history or family mental health history.

This Report further demonstrates that the U.S. military knew, and any competent medical professional would have known, of the severe side effects caused by mefloquine:

- Mefloquine was first developed by the United States military.
- Mefloquine is a quinolone, a drug family the CIA experimented with under a project called MKULTRA that studied psychotropic drugs for behavioral modification for use as a weapon and interrogation tool.
- As of 2002, Roche USA, the manufacturer of mefloquine under the brand name Lariam, warned of its contraindications and at least some of its severe side effects on the drug’s package insert.
- Beginning at least as early as 1990, multiple peer-reviewed medical studies documented the severe adverse effects associated with mefloquine.

While it is impossible to make definitive conclusions as to the purposes for this policy without additional information, particularly detainee medical records, the available evidence may support one of several possible conclusions:
• Gross medical malpractice: If government intended this mefloquine regime for malaria treatment and control, it was done in a manner that jeopardized the health and perhaps the lives of the detainees and that violated basic standards of medical care.

• Mefloquine was given in order to bring about the adverse effects for one of three reasons. Any of these would likely satisfy the legal definition of torture as articulated by the Department of Justice in 2002.
  o As part of a program of enhanced interrogation, the psychotropic effects of mefloquine may have been intended as an aid to breaking a detainee’s resistance. This would be the psychological equivalent of waterboarding.
  o As part of an experimental study to gather data on the side effects of mefloquine.
  o As a punitive measure.

Methodology

This Report documents the administration of mefloquine to detainees and establishes that the U.S. military’s administration was a violation of normal standards of medical care. The Center for Policy and Research at Seton Hall School of Law typically issues reports based on government documents. In this case, however, that has proved impossible because the government has continually refused to release detainee’s medical records to the detainees or their attorneys. The only medical record available is that of ISN 693. Additionally, two pages of the inprocessing form for ISN 760 are available and were analyzed. In order to supplement these sources, the Center’s Research Fellows analyzed other publicly-available documents. These include contemporaneous statements by government authorities regarding malaria treatment practices at GTMO, Standard Operating Procedures, and published, peer reviewed medical studies.

I. Mefloquine was not given to detainees in a manner consistent with malaria treatment.

Mefloquine is an antimalarial drug that can be used for prophylaxis or for treatment with different dosages and administration for each. The dosage administered and the timing of each
dose of mefloquine to detainees suggests that the military may have used it for treatment purposes without first ascertaining whether the detainee actually had malaria. It is highly likely that the military was treating uninfected individuals with high doses of a dangerous drug.

The prophylactic dosage of mefloquine, 250 mg, is much smaller than the treatment dose given to GTMO detainees, 1250 mg, and is administered once per week as opposed to the single dose\(^1\) used for treatment purposes.\(^2\) Severe adverse side effects do occur during prophylactic use, but adverse effects during use for treatment are far more common and more severe, probably due to the larger dosage. Use of mefloquine, even when used to treat a confirmed case of the disease, is contraindicated\(^3\) when the patient has a history of certain disorders.\(^4\)

Detainees were given 1250 mg of mefloquine during inprocessing at GTMO; 750 mg as an initial dose and 500 mg 12 hours later.\(^5\) There is no indication that the routine administration of mefloquine to arriving detainees considered each detainee’s medical history.\(^6\) Administering the drug at the higher treatment dose without previously determining the need for any treatment was a dramatic departure from the accepted standard of medical care.\(^7\)

Doctors have widely prescribed mefloquine, commercially sold as Lariam by manufacturer Roche USA, throughout the United States and elsewhere as a prophylactic against malaria infection. Mefloquine is particularly effective in preventing malaria in areas where the

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1. The 1250 mg treatment dose can be split into two parts, 750 mg and 500 mg, given 6-12 hours apart. *See, e.g.*, Lariam Label, Roche USA.
2. Lariam Label, Roche USA.
3. A contraindication is “a factor that prohibits administration of a drug or the performance of an act or procedure in the care of a specific patient.” *Mosby’s Dict. of Med., Nursing, & Health Prof’s 454 (7th ed. 2006)* [hereinafter Mosby’s].
4. Lariam Label, Roche USA.
5. *See Part II, infra.*
6. *Id.*
disease-causing parasite has developed resistance to cloroquine. Mefloquine kills the parasites that cause malaria. Specifically, mefloquine acts as a blood schizonticide, selectively destroying multinucleate sporozoa of parasites in the blood; however the exact mechanism of action is unknown. Mefloquine can cross the blood-brain barrier, and has a relatively long half-life at 15 to 33 days until elimination. This means that the drug can enter brain tissue and remains in the body for a long period of time. As Dr. G. Richard Olds, an internationally recognized tropical disease specialist and Founding Dean of the University of California at Riverside School of Medicine, told the Center, “Mefloquine is fat soluble and as a result it does build up in the body and has a very long half-life. This is important since a massive dose of this drug is not easily corrected and the ‘side effects’ of the drug could last for weeks or months.” Dr. Olds’s view is well supported by the medical literature reviewed by the Center for this Report.

The recommended prophylactic adult dosage for mefloquine is 250 mg taken once per week, beginning one week before travel to a malaria zone and continuing until four weeks after exposure to a malaria zone has ended. For mild to moderate cases of malaria diagnosed in adults, a treatment dosage of 1250 mg is indicated when the malaria strain is caused by P. vivax or mefloquine-susceptible strains of P. falciparum.

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8 Eric Woolorton, Mefloquine: contraindicated in patients with mood, psychotic or seizure disorders, CANADIAN MED. ASS’N J. (Nov. 12, 2002).
9 Lariam Label, Roche USA.
10 Id.
11 Francois Nosten & Michele van Vugt, Neuropsychiatric Adverse Effects of Mefloquine: What Do We Know and What Should We Do?, CNS DRUGS, Jan. 11, 1999, at 5.
12 Lariam Label, Roche USA.
A. Side Effects Can Be Severe

Mefloquine, at any dose, is known to cause adverse neuropsychiatric effects such as anxiety, paranoia, hallucinations, aggression, psychotic behavior, mood changes, depression, memory impairment, convulsions, loss of coordination (ataxia), suicidal ideation, and possibly suicide.\(^\text{14}\) As many as 25% of persons who have taken mefloquine reported such severe side effects.\(^\text{15}\) These neuropsychiatric side effects are more prevalent and more severe in patients with a history of certain disorders and conditions or when taken in combination with certain medications, requiring careful prescribing that is dependent on a thorough and complete review of each patient’s medical history.\(^\text{16}\)

A U.S. military service member reported the following adverse effects from a weekly regimen of mefloquine at the lower prophylactic dosage.\(^\text{17}\) The adverse effects began soon after the first dose, and gradually grew worse as more doses were taken.\(^\text{18}\) Though he took the drug for only six months, his symptoms persisted for well over a year after his last dose.\(^\text{19}\) He reported:

*Anger, insomnia, and paranoia. My eyes started giving out. Had to wear reading glasses to see my computer... Had an intense bout of vertigo during a live fire exercise at night. Became very ill after seeing intense flashes of lights*


\(^\text{16}\) Remington L. Nevin et al., Prevalence of contraindications to mefloquine use among USA military personnel deployed to Afghanistan, *MALARIA J.* (Feb. 11, 2008), http://malariajournal.com/content/7/1/30. 

\(^\text{17}\) Confidential email from United States Naval Commander, Retired to Prof. Mark Denbeaux (Nov. 2, 2010). 

\(^\text{18}\) *Id.* 

\(^\text{19}\) *Id.*

Anecdotal evidence also indicates auditory and visual illusions have been reported during adverse events.21 Many are described as “zooptia,” meaning the patient sees animals, while other descriptions have centered on death figures, such as the grim reaper. Adverse effects are similar, though more common and more severe, at the higher treatment dosage.22

The product label for Lariam also contains the following warnings:

- **In patients with epilepsy, Lariam may increase the risk of convulsions. The drug should therefore be prescribed only for curative treatment in such patients and only if there are compelling medical reasons for its use.**

- **Lariam should be used with caution in patients with psychiatric disturbances because mefloquine use has been associated with emotional disturbances.**

- **The benefits of Lariam therapy should be weighed against the possibility of adverse effects in patients with cardiac disease.**

- **Do not take Lariam if you have:**
  - depression or had depression recently
  - had recent mental problems, including anxiety disorder, schizophrenia, or psychosis (losing touch with reality)
  - seizures or had seizures (epilepsy or convulsions)
  - an allergy to quinine, quinidine, Lariam or any ingredients in Lariam.23

These warnings reflect studies confirming the potential for severe side effects associated with Lariam. A 1999 study documented over 150 clinical presentations of neuropsychiatric

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20 *Id.*
21 Email from Major Remington Nevin, M.D. to Prof. Mark Denbeaux (Nov. 7, 2010).
22 See *infra* Part I.A.
23 Lariam Label, Roche USA.
effects of mefloquine. The study cited to multiple other studies that identified predisposing factors to the occurrence of these effects, such as a family history or a past history of neuropsychiatric disorders or recent previous exposure to mefloquine or use of psychotropic drugs; it urged that mefloquine should not be used by patients who are so predisposed. It is “clear,” therefore, “that mefloquine is contraindicated for people with a recent history of depression, generalized anxiety disorder, or a psychotic or seizure disorder,” as well as people with a family history of mental illness. The effects can be long lasting, as mefloquine can cross the blood-brain barrier and accumulate in brain tissue. 

One study specifically and strongly recommends against “the practice of mass-prescribing mefloquine without an individualized review of medical records,” and calls for thorough counseling before giving a patient the drug. Considering the array of strong warnings concerning prescribing mefloquine, it is a very dangerous drug.

B. Driven to Psychosis: Risks Rise With Dosage Levels

The recommended prophylactic adult dosage for mefloquine is 250 mg taken once per week. A treatment dosage of 1250 mg is indicated for mild to moderate malaria in adults caused by P. vivax or mefloquine-susceptible strains of P. falciparum, unless previous prophylaxis with mefloquine has failed. Therefore, mefloquine is not appropriate for use in

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24 Nosten & van Vught, supra note 11, at tbl. 1; see infra App’x A.
25 Id. at 1, 4.
26 Eric Wooltorton, supra note 1.
27 Id. at 5.
28 Remington L. Nevin, supra note 8.
29 Tuan M. Tran et al., supra note 13; see also Lariam Label Update, supra note 13.
30 Id.
treatment of (1) severe cases of malaria, (2) cases of malaria not caused by these two parasites, or (3) patients who had previously taken mefloquine for prevention of malaria.

The frequency and severity of adverse effects increases dramatically at the higher treatment dosage. A survey of 20 published prospective studies of mefloquine administered at the treatment dosage of 1250 mg concluded that “the incidence of serious neuropsychiatric reaction is higher when mefloquine is used for treatment rather than prophylaxis” and that the risk is dose-dependent. The profiles of adverse events in those instances were similar to those under prophylactic use; the risk factors and adverse effects remained the same. Another study of healthy individuals who took the treatment regimen at the same dose given to the detainees (1250 mg) found an unexpected high frequency of side effects reported by all 22 subjects, with symptoms lasting three weeks or longer.

This finding is corroborated by a case study of serious adverse effects suffered by a patient who took a 1250 mg therapeutic dose of mefloquine. A patient was driven to mefloquine-induced psychosis by a single 1250 mg dose, a psychosis that lasted for weeks. Within a day of taking the medication, the patient experienced vertigo and insomnia. Days later, he was experiencing anxiety and nervousness, and began to have unusual conversations about spirituality and religion with his wife. He began to have difficulty following conversations and became suspicious of his wife’s fidelity without reason. After two weeks of

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31 Francois Nosten & Michele van Vugt, supra note 24.
32 Id.
34 Tuan M. Tran et al., supra note 13.
35 Id.
36 Id.
37 Id.
38 Id.
taking the dose, the patient was anxious, agitated, and delusional.\textsuperscript{39} He exhibited paranoia and agitation upon admission to the hospital.\textsuperscript{40} He reported suicidal ideation and attempted to escape from the hospital.\textsuperscript{41} Hospital staff had to place him in restraints due to “profound psychomotor agitation.”\textsuperscript{42} He was medicated for acute psychotic agitation.\textsuperscript{43} For six days after admission, the patient was argumentative with staff and resisted treatment, remaining agitated and delusional.\textsuperscript{44} Finally, he submitted to medication and his symptoms abated somewhat, though he still had trouble following conversations.\textsuperscript{45} The case study concluded that physicians should carefully assess patients before prescribing mefloquine and should monitor the patient after the treatment dose, intervening if necessary to avoid severe psychosis.\textsuperscript{46} The study also urged doctors to advise patients of the possible side effects so they can recognize symptoms when they arise.\textsuperscript{47}

II. Mefloquine Was Given to Detainees Without Regard for Necessity or Contraindications

Upon a detainee’s arrival at GTMO, military personnel administered 1250 mg of mefloquine to each detainee as part of standard in-processing orders, according to GTMO Medical Standard Operating Procedures (SOPs).\textsuperscript{48} This is corroborated in practice by government medical records for two detainees.\textsuperscript{49} Very few medical records have ever been

\textsuperscript{39} \textit{id.}
\textsuperscript{40} \textit{id.}
\textsuperscript{41} \textit{id.}
\textsuperscript{42} \textit{id.}
\textsuperscript{43} \textit{id.}
\textsuperscript{44} \textit{id.}
\textsuperscript{45} \textit{id.}
\textsuperscript{46} \textit{id.}
\textsuperscript{47} \textit{id.}
\textsuperscript{49} ISN 693, Medical Files folder 1 of 3 Guantanamo Bay, Cuba 3 detainees deaths investigation, June 10, 2006, at 18, 187 [hereinafter ISN 693 Med Files], \textit{available at}
released for GTMO detainees, and those the government has released are heavily redacted and may be incomplete.\textsuperscript{50} Based on the documents that are available, however, it is clear that detainees have been given a high dose of this powerful anti-malarial drug that potentially causes severe neuropsychological side effects. Since the dosage far exceeds the recommended dose for prophylactic purposes, the only medical justification would be particularized reason to believe the detainees were suffering from malaria. Further, while at least some detainees were tested for malaria, the mefloquine was seemingly administered in advance of and without regard to the results of the test. In any event, there does not appear to have been any individualized assessment of medical and psychological history prior to mefloquine administration for the purpose of avoiding administration to detainees with contraindications to mefloquine, which would render the administration of the drug inappropriate even if malaria infection were confirmed.

\textbf{A. Empiric Therapy: Risks Outweigh Potential Benefits}

GTMO Medical SOP 021, entitled “Infection Control,” states that a 1250 mg dose of mefloquine will be included in “empiric therapies.”\textsuperscript{51} An empiric therapy is the initiation of treatment in the absence of or prior to diagnosis.\textsuperscript{52} For example, if a high school student died of meningitis, an empiric approach may be taken with his classmates, under which all would

\textsuperscript{50} It is unclear why the U.S. government has continually refused to release medical records for detainees upon request of the detainees or their lawyers.

\textsuperscript{51} \textit{See SOP 021, supra note 48}. The empiric therapies also include albendazole at 400 mg, a dosage used to treat filaria. This also appears on the Standard Inprocessing Form, as item “2.” just after the 1250 mg dose of mefloquine. ISN 693 Med Files, \textit{supra} note 49.

\textsuperscript{52} MOSBY’S, \textit{supra} note 3, at 1887.
immediately be given a wide-spectrum antibiotic without waiting for a test result. This approach is used because the risks of not treating or of waiting for diagnosis outweigh the risks of immediate treatment. Employment of empiric therapy for malaria in these cases with any drug, let alone a drug with severe adverse effects such as mefloquine, violates recommended practices in the field of tropical disease medicine. Mefloquine is also inappropriate in such a regime because it is not indicated for treatment of severe or life-threatening malaria, so the potential benefits of a presumptive treatment with mefloquine would never outweigh the risks.

The Centers for Disease Control (CDC) does not recommend empiric treatment for persons from Afghanistan or Pakistan, where a majority of the detainees were captured. The CDC recommends such treatment only for persons who (1) are from sub-Saharan Africa because in that region, it is common for persons to have the deadliest form of malaria, P. falciparum, but show no symptoms, and (2) who do not have any contraindications to the treatment drug. The CDC lists three empiric treatment options for persons from sub-Saharan Africa; none utilize mefloquine as the treatment drug.

Empiric treatment is improper in persons from South Asia because it is rare for persons coming from South Asia to have asymptomatic or sub-clinical P. falciparum malaria infection. In these latter populations, “the risk and cost of post-arrival presumptive treatment currently outweighs the potential benefits. . . . However, any refugee from an endemic area with signs or symptoms of malaria should be receiving diagnostic testing for Plasmodium and subsequent

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54 Id.
55 Id.
treatment for confirmed infections.” Therefore, the CDC calls for testing, and treatment only for confirmed infections. British experts concur: “If malaria is suspected, a blood test for malaria without delay is mandatory. . . . Empirical therapy for malaria should not be given unless a patient with a convincing exposure history demonstrates features of severe malaria and expert advice has been taken.” Even in those circumstances, however, mefloquine would not be the appropriate drug because it is not used to treat severe cases of malaria.

Despite professional medical/health organizations denouncing the use of mefloquine for empiric treatment, U.S. Military SOPs at GTMO mandated that detainees receive a full treatment dose of 1250 mg of mefloquine upon arrival.

Interestingly, the statements of a Navy preventative medicine specialist cast doubt as to whether this SOP accurately reflects the policy of the Navy and calls into question the purposes for that policy. At a 2002 meeting of the Armed Forces Epidemiological Board (AFEB), the Navy said that the malaria policy in GTMO involved use of insect repellents such as permethrin and Deet to keep mosquitoes away from detainees, adulticiding and larvaciding the area to reduce the number of mosquitos, and using Primaquine as a gametocidal agent to prevent transmission. When asked directly about efforts to deal with malaria at GTMO, the Navy’s liaison officer to the AFEB, Captain Alan “Jeff” Yund, did not mention mefloquine at all. Captain Yund did say that an unspecified number of detainees arrived with malaria parasites in

56 Id.
58 See SOP 021, supra note 48, at 81.
59 Meeting Minutes, U.S. Armed Forces Epidemiological Board (Feb. 19, 2002), at 109–110 (on file with the Center).
60 Id.
their blood.\cite{Id. at 107.} He stated that the Navy wanted to “treat the malaria that the individual detainee has,” indicating that treatment is based on an individual assessment and directed at those who actually have malaria.\cite{Id.} Captain Yund also said that because malaria has been absent from Cuba for quite some time, that for the Navy, “another big issue is doing what’s necessary to prevent malaria from becoming endemic in this area again.”\cite{Id.} Empiric treatment was never mentioned and would contradict Captain Yund’s statement about individualized treatment.

B. The Standard In-processing Orders Form

Mefloquine was given to each detainee as a matter of standard procedure without waiting for the results of any test for malaria. This is further made clear by an examination of the “Standard In-processing Orders” form, presumably applied uniformly for all detainees.\cite{Id.} The form includes administration of mefloquine at the 1250 mg dosage, split into two distributions: “750 mg PO [taken orally] now, 500 mg PO in 12 hours.”\cite{Id.}

The form is structured as a checklist, with numbered items circled as they were completed. The first item on the list is “1. Mefloquine,” followed by the dosage.\cite{Id.} On both ISN 693’s form and ISN 760’s form, number “1.” is circled, indicating the mefloquine dose was administered.\cite{Id.}

\begin{itemize}
\item \cite{Id. at 107.}
\item \cite{Id.}
\item \cite{Id.}
\item \cite{See supra note 49.}
\item \cite{Id.}
\item \cite{Id.}
\item \cite{Id.}
\item \cite{Id.}
\end{itemize}
It is true that the form requires testing for malaria. Under number “4. LABS,” there appears “Malaria Smear and PCR.”\(^{68}\) PCR is the abbreviation for “Polymerase Chain Reaction,” a method of testing for malaria parasites.\(^{69}\) There is no indication on the form that the 1250 mg dose of mefloquine should be given after the malaria tests have been performed, nor that giving the mefloquine is contingent upon a positive malaria test. There is no space on the form to list the results of the malaria tests. Item number “4.” is circled on ISN 693’s form but not on ISN 760’s form, which may indicate that in the latter case, the tests were not performed.\(^{70}\) Nothing on the form requires detainees to be warned of possible side effects or instructed to immediately report any adverse effects.

To the contrary, the relative positions of the mefloquine dosage and the malaria tests on the checklist suggests that the mefloquine is to be given to every detainee as a matter of course, prior to malaria testing. Mefloquine is number one on the checklist; the malaria tests are the fourth lab test listed under item number four on the checklist. The form does not ask for input as to the positive or negative result of the malaria test and does not state that mefloquine is to be given only if the detainee has malaria.

This inference is confirmed by the Chronological Record of Medical Care, wherein the use of another malaria drug is made contingent on a blood test.\(^{71}\) If a detainee is not G6PD deficient,\(^{72}\) the detainee is given Primaquine.\(^{73}\) If the detainee is G6PD deficient, the detainee is

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\(^{68}\) Id.

\(^{69}\) MOSBY’s at 1413, 1490.

\(^{70}\) See supra note 49.

\(^{71}\) See ISN 760 Med Files, supra note 49; see infra App’x B.

\(^{72}\) Glucose-6-phosphate dehydrogenase (G6PD) deficiency is “an inherited disorder characterized by red cells partially or completely deficient in G6PD, an enzyme critical in aerobic glycolysis.” MOSBY’s, supra note 3, at 816. Those with the disorder may experience episodes of acute hemolysis (breakdown of red blood cells) due to exposure to certain drugs. Id.

\(^{73}\) See ISN 760 Med Files, supra note 49; see infra App’x B.
instead given Chloroquine.\textsuperscript{74} Thus, if the administration of a drug were to be contingent upon the results of a blood test, the Standard Orders would presumably make that clear in the forms. The administration of mefloquine, however, is not conditioned on positive malaria test results.\textsuperscript{75} The conclusion is inescapable that mefloquine is given to each detainee as a matter of standard operating procedure.

Likewise, there is no item on the checklist for a medical history to ascertain whether the detainee has a past history or a family history of neuropsychiatric disorders or recent previous exposure to mefloquine or use of psychotropic drugs. Nowhere in the available detainee medical records is there any indication that such a history was taken at any time as a part of the standard in-processing procedures, either before or after the detainee was given mefloquine.

Further, there is evidence in the records that in at least one case, when a detainee presented with symptoms that may have indicated an adverse reaction to the drug, mefloquine was never indicated to be a possible cause. ISN 693 was given 1250 mg of mefloquine beginning on June 18, 2002.\textsuperscript{76} On July 1, 2002, two weeks after the mefloquine administration, he was interviewed—presumably by a counselor, though the identity is redacted—because he was refusing to eat.\textsuperscript{77} The interviewer noted that the detainee reported he had previously been treated for anxiety and that his father had a history of mental illness.\textsuperscript{78} These are both red flags of contraindication for mefloquine use.\textsuperscript{79} The detainee complained of sleep loss due to anxiety, shortness of breath due to anxiety, nightmares, and suicidal thoughts; all symptoms that fall

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\textsuperscript{74} \textit{Id.}
\textsuperscript{75} \textit{See supra} note 49.
\textsuperscript{76} ISN 693 Med Files, \textit{supra} note 49, at 18; \textit{see infra} App’x B.
\textsuperscript{77} \textit{Id.} at 127.
\textsuperscript{78} \textit{Id.}
\textsuperscript{79} Lariam Label, Roche USA.
within the possible adverse effects of mefloquine use.\textsuperscript{80} The detainee was then diagnosed with adjustment disorder with anxiety and passive-aggressive personality traits.\textsuperscript{81} The only follow-up prescribed at that time was to encourage food and fluid intake to end his hunger strike and to monitor for changes in condition or self-harming behavior.\textsuperscript{82} Mefloquine was not mentioned in the evaluation.\textsuperscript{83}

Two days later, a note was made in ISN 693’s file that he was still having thoughts of suicide but indicated that “It is against my religion.”\textsuperscript{84} He presented with auditory and visual hallucinations of “voices and the ceiling coming down” on him and again, reported sleep broken by nightmares.\textsuperscript{85} He also suffered decreased appetite and concentration.\textsuperscript{86} These symptoms are consistent with adverse effects of mefloquine use, but, again, the medical record makes no mention of mefloquine.\textsuperscript{87}

These interviews are also significant because in June of 2006, after ISN 693 died, the Senior Medical Officer (SMO) of GTMO stated in an official document that ISN 693 had “[n]o known psychiatric history.”\textsuperscript{88} In the same document, the SMO refers to a July 2002 treatment ISN 693 received for a mandibular abcess/cyst, indicating that the SMO was familiar with ISN 693’s medical records for the same period of time as the interviews where he reported psychiatric symptoms.\textsuperscript{89} That the SMO did not consider that suicidal thoughts, anxiety, and

\textsuperscript{80} Id.
\textsuperscript{81} Id.
\textsuperscript{82} Id.
\textsuperscript{83} Id.
\textsuperscript{84} ISN 693 Med Files, supra note 49, at 127; see infra App’x B.
\textsuperscript{85} Id.
\textsuperscript{86} Id.
\textsuperscript{87} Id.
\textsuperscript{88} Senior Medical Officer, Narrative Summary (June 10, 2006) (on file with Center).
\textsuperscript{89} Id.
nightmares amounted to a psychological history is puzzling unless perhaps the SMO believed that these symptoms were caused by mefloquine.

C. No Malaria In Cuba

According to the Centers for Disease Control and Prevention, there is no malaria in Cuba.\textsuperscript{90} “Malaria is not a threat in Guantanamo Bay,” according to an official memorandum on the “Department of Defense Operational Use of Mefloquine.”\textsuperscript{91} U.S. military personnel and contractors are not prescribed any anti-malarial medication for assignment to GTMO.\textsuperscript{92}

Because GTMO is not a malaria zone, administration of mefloquine is not indicated for prophylactic use. That fact, coupled with the high dose given to detainees, indicates that the mefloquine administered would have been justified, if at all, only for treatment purposes. But mefloquine is only to be used as a treatment drug for mild to moderate cases of malaria caused by certain parasites and only for patients for whom contraindications do not suggest that the risks may outweigh the benefits.\textsuperscript{93} This raises the question of why mefloquine was given to every detainee without first determining whether he had malaria or not and without taking a medical history first.

III. The Military Was Aware of the Dangerous Effects of Mefloquine

The U.S. military was aware of the risk of severe adverse neuropsychological effects of mefloquine before the establishment of the GTMO detention facility. As early as 1955, and

\textsuperscript{90} Centers for Disease Control and Prevention, \textit{Malaria Information and Prophylaxis, by Country} (Sep. 21, 2010), \textit{available at} http://www.cdc.gov/malaria/travelers/country_table/c.html.

\textsuperscript{91} Letter from William Winkenwerder, Jr., M.D., to Hon. John M. McHugh (Sep. 13, 2002) (on file with Center).

\textsuperscript{92} \textit{id}.

\textsuperscript{93} Lariam Label, Roche USA.
possibly earlier, the CIA was experimenting with quinolines, the chemical family to which mefloquine belongs, as part of MKULTRA, a program of research in behavioral modification. Quinolines were included in a study of the “curare-like”—a type of poison used on native blow darts—effects of thiols, and another study that investigated toxic cerebral states. The stated aim of the latter study was to “understand the mechanism of such states as toxic delirium, uremic coma, and cerebral toxicity from poisoning.” The potential use of these drugs in an interrogation setting was a stated purpose for the study: “an adversary service could use such drugs to produce anxiety or terror in medically unsophisticated subjects unable to distinguish drug-induced psychosis from actual insanity.”

From this family of chemicals, mefloquine was developed under the U.S. Army Antimalarial Drug Development Program in the 1960s. At least as early as 1991, neuropsychiatric adverse effects of therapeutic doses of mefloquine had been reported in scientific studies. In 1993, Senator Dianne Feinstein asked the Pentagon to look for alternatives to mefloquine after media reports cited possible links between Lariam and suicides and other erratic behavior. In 2002, Dr. William Winkenwerder, the Assistant Secretary of

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94 Project MKULTRA, The CIA’s Program of Research in Behavioral Modification: Joint Hearing Before the Select Committee on Intelligence and the Subcommittee on Health and Scientific Research 95th Cong. 193–96 (1977). This hearing dealt with illegal and unethical experiments performed by the CIA in the 1950s and 1960s. Projects included enticing heroin addicts to experiment with LSD in order to earn heroin and giving LSD to unsuspecting citizens in various social situations.

95 Id.
96 Id. at 195.
97 Id. at 221.
98 Chansuda Wongsrichanalai et al., Mefloquine—Its 20 Years in the Thai Malaria Control Program, 35 SOUTHEAST ASIAN J. TROPICAL MED. PUB. HEALTH 300, 300 (2004). Wongsrichanalai is a member of the U.S. Army Medical Component, Armed Forces Research Institute of Medical Sciences.
99 Chansuda Wongsrichanalai, supra note 22 at 301.
100 Kelly Kennedy, supra note 15.
Defense for Health Affairs, acknowledged that concerns had been raised by peer-reviewed reports that adverse event rates were much higher than previously reported.\textsuperscript{101} Dr. Winkenwerder reiterated that “health care providers, including those within the DoD, must weigh the benefits of the drug against the possibility of adverse reactions in some individuals.”\textsuperscript{102} This was to be done in part by considering “the severity of the disease, characteristics unique to the patient to whom they are prescribing the drug, [and] other medications the individual might be taking.”\textsuperscript{103} The Defense Department was further aware that “sufficient evidence exists [in 2002] to raise the question whether the neuropsychiatric adverse events of mefloquine are frequent enough and severe enough to warrant limiting its use for the prevention and treatment of chloroquine-resistant malaria.”\textsuperscript{104} Because the most “severe adverse events reported with mefloquine have occurred during its use as treatment for documented infection with chloroquine resistant P. falciparum, other treatment regimens should be carefully considered before mefloquine is used at the doses required for treatment.”\textsuperscript{105} The sources cited by that Department of Defense memo were studies ranging from 1989 to 2001.\textsuperscript{106}

IV. Mefloquine and Torture?

Unfortunately the GTMO mefloquine standard operating procedure raises the possibility of abuse and torture that shadows any discussion about detainee treatment at the facility. In a memorandum prepared by Assistant Attorney General Jay Bybee for Attorney General Alberto Gonzalez (“the memo”), the Justice Department developed its official stance on the legal

\textsuperscript{101} See supra note 91.
\textsuperscript{102} Id.
\textsuperscript{103} Id. at 21–22.
\textsuperscript{104} Id.
\textsuperscript{105} Id.
\textsuperscript{106} Id.
definition of torture and the interpretation of 18 U.S.C. §§ 2340-2340A.\textsuperscript{107} Section 2340A
criminalizes torture outside the United States, and § 2340 defines torture as an
act committed by a person acting under the color of law specifically intended to
inflict severe physical or mental pain or suffering (other than pain or suffering
incidental to lawful sanctions) upon another person within his custody or physical
control.\textsuperscript{108}

To violate § 2340A, the severe pain and suffering must be inflicted with specific intent, which
the memo interprets to mean that the infliction of pain must be the defendant’s precise
objective.\textsuperscript{109} The memo points out that, although knowledge alone that an action is certain to
cause severe pain and suffering does not constitute specific intent, “juries are permitted to infer
from factual circumstances that such intent is present.”\textsuperscript{110} “Therefore, when a defendant knows
that his actions will produce the prohibited result, a jury will in all likelihood conclude that the
defendant acted with specific intent.”\textsuperscript{111}

The statute defines “severe mental pain or suffering” to include, in relevant part, “the
prolonged mental harm caused by or resulting from . . . the administration or application, or
threatened administration or application, of mind-altering substances or other procedures
calculated to disrupt profoundly the senses of the personality.”\textsuperscript{112} The memo stresses that
because the statute specifies “prolonged” harm as a prerequisite to conviction, a specific intent to
cause prolonged harm would be required as well.\textsuperscript{113}

\textsuperscript{107} Memorandum for Alberto Gonzales on Standards of Conduct for Interrogation Under 18
\textsuperscript{108} \textit{Id.}
\textsuperscript{109} \textit{Id.} at 3.
\textsuperscript{110} \textit{Id.} at 4.
\textsuperscript{111} \textit{Id.}
\textsuperscript{112} \textit{Id.} at 6.
\textsuperscript{113} \textit{Id.} at 8.
The memo outlines a good faith defense, arguing that if a defendant acted with a good faith belief that his conduct would not produce the illegal result, he cannot have acted with specific intent.\textsuperscript{114}

The memo analyzes the statute’s use of the phrase “mind-altering substances or other procedures” and concludes that this language refers to drugs or actions that profoundly disrupt the personality.\textsuperscript{115} The memo argues that the statute contemplates drugs and actions that “penetrate to the core of an individual’s ability to perceive the world around him, substantially interfering with his cognitive abilities, or fundamentally alter his personality.”\textsuperscript{116} It states that “the onset of ‘brief psychotic disorder’ would satisfy this standard.”\textsuperscript{117} The standard could also be satisfied by delusions or hallucinations lasting as short as one day.\textsuperscript{118} The memo also cites, as an example of a profound disruption, a drug or action “pushing a person to the brink of suicide, particularly where the person comes from a culture with strong taboos against suicide.”\textsuperscript{119}

Section 2340A, consistent with the U.N. Convention Against Torture, proscribes these acts because they are the “most heinous acts,” the “most egregious conduct,” and “the worst forms of cruel, inhuman, or degrading treatment or punishment.”\textsuperscript{120}

In administering mefloquine to GTMO detainees in the manner at issue here, the government may have fallen within the DoJ’s definition of torture under § 2340. It is unknown from the available evidence whether the military gave mefloquine with the intent of causing severe neuropsychological side effects. However, it seems highly implausible that those who

\textsuperscript{114} Id. at 4.
\textsuperscript{115} Id. at 10–11.
\textsuperscript{116} Id. at 11.
\textsuperscript{117} Id. at 11.
\textsuperscript{118} Id.
\textsuperscript{119} Id.
\textsuperscript{120} Id. at 22.
authorized the program did not have full knowledge of the likelihood of adverse effects. Under the DoJ’s analysis, those individuals could be found to have the specific intent required, particularly because the drug was administered without regard to whether the detainees actually had malaria or whether they had a history or a family history of mental illness.

The government has had long experience with mefloquine and knew about the risks and that the risks greatly increase at the higher treatment dose. Indeed, the fact that the CIA was experimenting with mefloquine’s drug family as part of a program on behavior modification in the 1960s demonstrates that it was well aware of its potential to alter personality. This would negate the good faith defense.

The scientific evidence of the severe adverse effects of mefloquine and the available evidence regarding ISN 693 shows that the side effects of mefloquine may amount to a profound disruption of personality under the statute. The fact that mefloquine can cause psychotic episodes, sleep loss, anxiety, interference with cognitive ability, delusions, and hallucinations cannot be disputed. ISN 693 suffered from auditory and visual hallucinations, anxiety, and sleep loss. He was also pushed to consider suicide, despite the fact that suicide was against his religion. Because mefloquine has an unusually long half-life and can cross the blood barrier and enter the brain tissue, its effects are sufficiently “prolonged” to satisfy the statute’s requirement. Therefore, mefloquine would fit the definition of a mood-altering substance under the statute, according to the DoJ analysis, and its use would be impermissible if not for appropriate treatment or prophylactic purposes.
V. Conclusion

There is no valid medical justification for blanket administration of a high dosage of mefloquine without regard to whether the patient has malaria and without regard to whether the patient has a history of mental illness. As Dr. Olds told the Center, “In my professional opinion there is no medical justification for giving a massive dose of Mefloquine to an asymptomatic individual. I also do not see the medical benefit of treating a person in Cuba with a prophylactic dose of Mefloquine.” If mefloquine was not given to detainees for a valid medical purpose, and it was administered with full knowledge of the likelihood of adverse effects and the potential for severe adverse effects, it may be inferred that the side effects were the intended outcome. Under the government’s own legal analysis, this would constitute torture under U.S. law and under the U.N. Convention Against Torture. Until the government releases the complete medical records for all detainees, the legal implications of the military’s use of mefloquine at GTMO, the motives for adopting this policy, and the potentially serious medical impact on those who received the drug will remain hidden.
APPENDIX A

Table of Adverse Effects Caused by Mefloquine

Source: Francois Nosten & Michele van Vugt, *Neuropsychiatric Adverse Effects of Mefloquine: What Do We Know and What Should We Do?*, CNS DRUGS, Jan. 11, 1999 at tbl. 1.
<table>
<thead>
<tr>
<th>Major psychiatric disorders and symptoms</th>
<th>Delirium, delusion, hallucinations, illusions, megalomania, paranoia, psychosis, schizophrenia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disorders of affect</td>
<td>Aggression, behaviour disturbance, character change, depersonalisation, depression, euphoria, hypomania, logorrhea, mania, mood swings, oppression, personality disorder, suicidal, suicide attempt</td>
</tr>
<tr>
<td>Neurosis</td>
<td>Hypochondriasis, malaise, mutism</td>
</tr>
<tr>
<td>Other psychiatric symptoms</td>
<td>Abnormal hunger, agitation, aggravation, amnesia, angor mortis (the feeling of imminent death), anorexia, anxiety, apathy, asthenia, disturbed awareness, reduced concentration, confusion, dazed, disorientation, dreams, drunken state, excitement, exhaustion, fatigue, fear, hyperventilation, insomnia, memory impairment, nervous, nightmares, panic reaction, restless, somnolence, speech disturbance, sweating, tiredness, decreased alertness, vegetative dystonia, weakness</td>
</tr>
<tr>
<td>Seizures</td>
<td>Aggravated seizure, convulsion, clonic seizure, epileptic seizure, epileptiform fits, generalised seizure, grand mal epilepsy, fits, tonic-clonic seizure</td>
</tr>
<tr>
<td>Disturbances in level of consciousness</td>
<td>Acute brain syndrome, cerebral oedema, cerebral ischaemia, clouded consciousness, coma, encephalopathy, encephalomyelitis, obturation, semi-conscious, stupor, unconscious</td>
</tr>
<tr>
<td>Dizziness</td>
<td>Abnormal cooordination, ataxia, balance disorder, dizziness, unsteady gait, lightheaded, loss of balance, uncoordination, vertigo, walking difficulties</td>
</tr>
<tr>
<td>Neuropathies</td>
<td>Anemia, cranial nerve disorder, abnormal EEG, twitching eyes, foot or hand paraesthesiae, general spasms, hearing disturbance, hypoesthesiae, leg paresis, leg pain, lip paraesthesiae, muscle weakness, myalgia, neurological disorder, neuropathy, numb fingers, numbness, paralysis, paraesthesiae, paresis, polyneuropathy, Raynaud’s syndrome, sensory disorder, slow reactions, tinnitus, tongue spasm, vision disturbance, weakness</td>
</tr>
<tr>
<td>Headache</td>
<td>Aggravated migraine, cephalgia, eye pain, headache, head pressure, migraine</td>
</tr>
<tr>
<td>Other neurological disorders</td>
<td>Abdominal pain, back pain, chest discomfort, chest pain, cramps, dystonia, fall, fever, gastric colic, hot flushes, incontinence, intestinal spasm, limb pain, lumbago, muscle tremor, oedematous legs, oesophageal burning, oropharyngeal spasm, pallor, rigors, shakiness, shivering, stomach pain, tetany, thirst, tinnitus, trauma, trembling, tremor, twitching, visual disturbance</td>
</tr>
</tbody>
</table>

**Table 1.** Various clinical presentations of neuropsychiatric effects of mefloquine. Exhaustive listing of reported adverse CNS reactions observed in people who received mefloquine[9]
APPENDIX B

Referenced Medical Files for ISN 693 and ISN 760.
STANDARD INTROCESSING ORDERS FOR DETAINEE:

1. Malachite 750 mg PO now, 500 mg PO in 12 hours
2. Alberdazole 400 mg PO once
3. Chest X-ray: PA
4. LABS:
   - Hep B surface antigen/antibody
   - Hep C - total
   - HIV
   - Malaria Smear and PCR
   - Hep A IgM
   - G6PD
   - Serum (draw 2 extra red tops)
   - Hep B core antibody

Circle if indicated:
1. AFB Smear QAM x 3
2. Td Smi IM once
3. Tetanus Ig 250 Units IM once
4. PPD - read in 48 to 72 hours
5. Additional Orders:

Staff Signature:

Signature:

(Medical Officer or Independent Duty Corpsman)

PATIENT'S IDENTIFICATION (Use this space for Mechanical Imprints)
STANDARD INTROCESSING ORDERS FOR DETAINERS:

1. Mefloquine 750 mg PO now, 500 mg PO in 12 hours
2. Albendazole 400mg PO once
3. Chest X-ray: PA

4. LABS:
   - Hep A IgM
   - Hep B surface antigen/antibody
   - Hep C - total
   - HIV
   - Malaria Sper and PCR

   Labs indicated:
   - AFB Smear QAM x 3
   - Td .5ml IM once
   - Tetanus 10 250 Units IM once
   - PPD - read in 48 to 72 hours

5. Additional Orders:

   [Signature]

   Staff Signature: [Signature]

   (Medical Officer or Independent Duty Corpsman)

PATIENT'S IDENTIFICATION (Use this space for Mechanical Imprint)

NAME: D.JTF 000 760

SSN: 888 00 0760

Slahi v. DoD (No. 06-CV-0597) - 3
STANDARD ORDERS FOR DETAINES:

1. If G6PD status has been documented as not deficient, give Primaquine 26.3 mg, 2 tabs PO qd X 14 days.

2. If G6PD status has been documented as deficient, give Chloroquine phosphate 500 mg 1 tab PO q week X 26 weeks.

3. Notify duty provider if patient refuses/misses 2 or more doses.

STAFF SIGNATURE: ___________________________