

**HIV Prevention Trials Network**  
**HIV 预防试验网络**

Clarification Memorandum # 1 to HPTN 058: A Phase III randomized controlled trial to evaluate the efficacy of drug treatment in prevention of HIV infection and death among opiate dependent injectors  
Final Version 2.0, 16 September 2008  
IND # 73,797

HPTN 058 澄清备忘录# 1 : 评价药物治疗对注射阿片类制剂预防 HIV 感染和死亡效果的 III 期随机对照临床试验

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*Section 1: Summary of Clarifications and Rationale*

*第一节 : 澄清和基本原理的总结*

The procedures clarified in this memorandum have been approved by the NIAID Medical Officer and are to be implemented immediately upon issuance. IRB approval of this Clarification Memorandum is not required by the sponsor; however, investigators may submit the clarification memo to the IRBs/ECs overseeing the study at their site for their information.

本备忘录中澄清的程序已被 NIAID 医疗官员批准，发布后立即执行。申办方不要求递交 IRB 审批此澄清备忘录；然而，研究者需要向所在现场的 IRBs/ECs 递交澄清备忘录备案。

Clarification is needed regarding the maximum allowable daily dosing for a participant. The original intent was to allow for physicians to set each participant's dose individually based on need. Section 4.3.3 could be mis-interpreted for a maximum daily dose of 16 mg.

关于参加者每日合理的最大赛宝松剂量的澄清是必要的。原来的意图是允许医生按照独特的的需要设定每位参加者的剂量。4.3.3 节可被错误解读为每日的最大剂量为 16mg.

No change in the informed consent form is necessitated by or included in this Clarification Memo.

本次澄清备忘录不涉及知情同意书的改变。

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## Section 2: Implementation

### 第二节：执行

The modifications detailed below will be incorporated into the next full protocol amendment. Text to be deleted is noted below by ~~strikethrough~~; text to be added is noted below in **bold**. 以下细节的修改将被纳入下一次完整的方案修订。删除的正文以删除线标识；增加的内容加粗标识。

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*This section should specify exactly where the protocol document will be modified to reflect the clarification when it is next amended.*

*本节必须明确指出在方案的下一次修订中，为反映澄清内容方案文件哪里将被修订。*

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#### 4.3.3 Treatment Dose and Administration

##### 4.3.3 治疗剂量和服用方法

##### Substitution Treatment Arm

##### 替代治疗组

Dosing will begin with a titration over a period of two to three days under supervision in the study clinic using the COWS as described above. On the first day of treatment, patients will initially receive a 4 mg dose of BUP/NX (expressed as the amount of buprenorphine) to be taken sublingually. Most participants will begin with a total first day's dosage of 8 mg. On Day 2, up to 16 mg may be given. Up to 32 mg may be given on Day 3 and thereafter until three-times-weekly dosing begins. The induction strategy is primarily dependent on three factors: 1) time since last opiate use; 2) type of opiate (e.g., long or short-acting) used; and 3) degree of physical dependence. Therefore, each dosing schedule will be tailored to the individual participant.

现场门诊根据上述 COWS 评分用 2-3 天时间进行精细的剂量调整。治疗第 1 天，参加者舌下含服 4 mg 的 BUP/NX (相当于丁丙诺啡的剂量)，绝大多数参加者第 1 天服药总剂量为 8 mg。第 2 天的总剂量可以调整到 16 mg，第 3 天的总剂量可以调整到 32 mg，直到确定每周 3 次服药剂量。导入期策略主要基于以下三个因素：1)距上次使用阿片类制剂的时间；2)阿片类制剂类型(长效或短效)；3)生理依赖水平。因此，应针对个体情况调整剂量。

Individuals randomized to the substitution treatment arm will come to the study site daily for direct observation of dosing until they have stabilized (for up to three weeks). Participants may be given a double dose or a take-home dose for days that the site is not staffed for dosing. After induction and stabilization, participants will be asked to come to the site for dosing three-times-weekly. **For example, the target dosage schedule for individuals whose daily dose was 16 to 24 mg/day or more is expected to be 32/32/48 mg administered on a three-times-weekly schedule (e.g., M/W/F); this is also the maximum three-times-weekly dosage. On rare occasions, for individuals who require more than 24 mg/day (i.e., 26, 28, 30, or 32 mg/day), it is unlikely that. In some individuals, the 32/32/48 mg three-times-**

**weekly** dosage schedule **may not** be adequate. For **such** individuals, as well as for others who received 24 mg or less per day but for whom the 32/32/48 mg three times weekly schedule is not adequate, dosing may be continued on a daily basis through Week 52 of the study, with take-home doses administered for those days on which in-clinic dosing is not possible (e.g., 32 mg on M/Tu/W/Th/F/Sat with a take-home 32 mg dose on Sun) **dosing may be observed in the clinic 4-times to 7-times per week during the maintenance phase as required for optimal treatment response. The maximum dose that may be administered at one time (i.e., to cover > 1 day) is 48 mg.** Participants receiving daily doses may also be given alternative day take home doses, which would conform to the visit schedule of those participants on three-times weekly dosing, at the discretion of the local investigators.

随机分到替代治疗组的研究对象每天要来门诊看服药物直到剂量稳定 (约三周)。如果发药人员缺勤, 可给参加者双倍剂量或一次的带药回家服用剂量。导入期或调整期后, 要求参加者每周三次回门诊服药。例如, 日剂量为 16-24mg/天或更高的剂量的参加者, 每周三次用药剂量和时间为 32/32/48mg (即: 周一/周三/周五)。这也是每周三次给药的最大剂量。个别案例, 每天服用剂量超过 24mg/天的人 (即 26、28、30 或者 32 mg/天), 对于一些参加者, 32/32/48mg 每周三次的用药方案可能不会满足其需求。对于这些参加者, 以及每天用药剂量为 24mg 或低于 24mg, 除一周 3 次的 32/32/48mg 用药方案不满足需求的参加者外, 建议用药治疗期间, 每天来门诊服药, 门诊休息日时, 则带药回家服用 (即, 周一/周二/周三/周四/周五/周六每天服用 32mg, 周日在家服用 32mg)。在维持治疗阶段, 参加者可每周 4 到 7 次来门诊服药已获得最佳治疗效果。在同一时间给予的最高剂量 (即, 覆盖 > 1 天) 是 48mg。每天用药的参加者亦可选择带药回家服用, 但需要与那些每周服药 3 次的参加者的方案一致, 由现场研究人员做出选择。