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Division of Dockets Management,
Food and Drug Administration,
Department of Health and Human Services,
5630 Fishers Lane, rm. 1061,
Rockville, MD 20852.

2013 AUG 12 P 12:43

Via Courier (DHL)

8 August 2013

Dear Sir or Madam

Citizen Petition – Use of Reglan in force-feeding at Guantánamo Bay

The petitioner is Corporate Social Responsibility Advocate at Reprieve, a legal action charity working to enforce the human rights of prisoners, including several of those incarcerated in Guantánamo Bay. As the Commissioner will be aware, there are currently widespread hunger strikes at Guantánamo. According to US military figures, at the date of filing 39 detainees are being enterally (forcibly) fed.[1]

This petition is submitted under §10.30 of Title 21 of the Code of Federal Regulations ("CFR"), and §355, §355-1, §372 and §393 of the Federal Food, Drug, and Cosmetic Act ("FDCA").

Further to the voluntary adverse incident report sent to the FDA on behalf of four Reprieve clients on 11 June 2013 (a copy of which is at Appendix 1), the petitioner requests the Commissioner to take urgent action to prevent any further forcible administration of Reglan, a drug regulated by the FDA, to hunger-striking detainees at Guantánamo Bay. As you will be aware, the prolonged use of Reglan risks causing serious and lasting side effects, including tardive dyskinesia, depression, thoughts about suicide and suicide.[2] This is of particular concern in the context of the force-feeding process, which has itself repeatedly been condemned by the medical profession as unethical and unjustifiable.

In particular, the petitioner requests that the conduct of ANI Pharmaceuticals, Inc., the only FDA-approved manufacturer of branded Reglan, be investigated and appropriate enforcement action be taken in respect of any breaches of the CFR or FDCA.

I. Action requested

The petitioner requests that the Commissioner takes the following actions:

(1) Suspends approval of Reglan for use in force-feeding at Guantánamo Bay as a matter of urgency due to the imminent hazard to the health of the detainees, pending completion of actions 2) and 3) below.

(2) Investigates the compliance of companies involved with supplying Reglan with the FDCA and CFR. This should include (without limitation) consideration of whether ANI Pharmaceuticals, Inc., its distributors, packers and/or authorized dispensers are failing to make Medication

[1] http://www.miamiherald.com/static/media/projects/gitmo_chart/
[2] http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/017854s058lbl.pdf; http://www.fda.gov/downloads/Drugs/DrugSafety/UCM235574.pdf

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Guides available to patients (or the patients' agents) in breach of 21 CFR 208.24. Following this investigation, the petitioner asks that the Commissioner takes all necessary enforcement action, which might include the issuance of public warning letters and/or notice of violation letters, against any companies found to be non-compliant.

(3) Assesses whether ANI Pharmaceuticals, Inc. should submit a new risk evaluation and mitigation strategy ("REMS") for Reglan under §355-1 FDCA. In particular, the Commissioner is requested to consider (without limitation) whether:

(i) a Communication Plan should be included in the REMS in accordance with §355-1(e)(3) FDCA, to ensure that information regarding Reglan is adequately communicated to health care providers; and

(ii) patients using Reglan should be subject to monitoring in accordance with §355-1(f)(3), to ensure that (a) Reglan is not taken for longer than the recommended 12-week period without a patient's informed consent; and (b) a patient's risk of depression and/or suicide is sufficiently low that the expected benefits of Reglan outweigh the potential risks.

II. Statement of grounds

A. Background

The Department of Defense's "Standard Operating Procedure for Medical Management of Detainees on Hunger Strike" ("SOP"), makes clear that Reglan is used in the force-feeding process. A copy of the SOP is enclosed at Appendix 2. It instructs medical staff who are force-feeding Guantánamo prisoners to use "Reglan 10 mg PO/enteral feeding tube Q 3 hr X 3 doses" where a detainee is nauseated or bloated after a tube is inserted for force-feeding.

Staff are also advised "to enhance gastric motility" in strikers by administering "Metoclopramide (Reglan) 10 mg via enteral feeding tube (place in feeding bag before nutritional supplement)". To be clear, 'intermittent feeding' is the US military euphemism for regular force-feeding of prisoners who have been checked out of hospital. This includes the majority of people being force-fed in Guantánamo. Critically, the SOP says nothing about side effects or informed consent – we believe consent is not sought before Reglan is administered.

As detailed in its FDA-approved labeling and Medication Guide[3], Reglan can cause serious side effects, including:

- tardive dyskinesia, a serious neurological disorder that is often irreversible, and the risk of which increases with duration of treatment and total cumulative dose;
- Uncontrolled spasms of face and neck muscles, or muscles of body, arms, and legs (dystonia);
- Depression, thoughts about suicide, and suicide;
- Neuroleptic Malignant Syndrome; and
- Parkinsonism.

[3] Appendix 3, also available at http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/017854s058lbl.pdf

Due to these side effects, the use of Reglan is not recommended for longer than 12 weeks. However, since force-feeding has been taking place at Guantánamo Bay since at least 4 March, it is highly probable that Reglan has been administered to some detainees for longer than this period. Given the risk of serious side effects associated with the prolonged use of Reglan, this constitutes an abuse of the drug which the FDA should take immediate action to prevent.

The medical profession overwhelmingly condemns the general practice of force-feeding hunger strikers as unjustifiable, unethical and counter-productive. The World Medical Association states unequivocally that force-feeding "*contrary to an informed and voluntary refusal*" is "*unjustifiable*", "*never ethically acceptable*" and that even if intended to benefit a person, is "*a form of inhuman and degrading treatment*".[4] The American Medical Association ("AMA") has repeatedly opposed force-feeding and urged the US government to abandon the technique. On 25 April 2013 the position was reinforced by Dr. Jeremy Lazarus, president of the AMA, in a letter to Defence Secretary Chuck Hagel.[5]

The Chairman of the British Medical Association has also written to President Obama and Mr Hagel, urging them to suspend immediately medical involvement in force-feeding at the Guantánamo Bay detention facility and to institute an urgent inquiry into how the situation was allowed to develop.[6] The BMA has also written to ANI Pharmaceuticals Inc, urging the company to take urgent practical steps to ensure that its medicines are used only for their intended medical purpose.

B. Misuse of Reglan at Guantánamo Bay

Administration of Reglan without informed consent

The 30-page SOP, despite its significant detail, makes no mention of Reglan's serious side effects or to obtaining the informed consent of detainees to its administration. Indeed, it is highly likely that detainees are not even aware that they are taking Reglan: the SOP provides that "*enteral feeding solutions will be prepared... out of the line of sight of detainees*" (p25).

Another section of the SOP provides "*standard responses*" for detainee questions/protests, and reads "*if the detainee attempts to slow the EF* [enteral feeding] *process by stating that the EF is infusing too fast, the nurse will reply: "The doctor has ordered some medication which may help with nausea; would you like me to administer it?"* (p26). The SOP instructs staff to use Reglan for nausea, yet this "script" makes no reference to informing the detainee of its side effects. There is therefore a serious risk that Reglan is being administered to detainees without their informed consent, particularly given the context of forced feeding.

Forcible use for longer than the recommended period

The SOP also makes no mention of restricting, or even monitoring, the length of time for which Reglan is administered. As the Medication Guide states, "*Your chances for getting tardive dyskinesia go up: the longer you take REGLAN and the more REGLAN you take. You should not take REGLAN for more than 12 weeks.*"

[4] Appendix 4.
[5] Appendix 5.
[6] Appendix 6.

Force-feeding of prisoners had begun by at least 4 March 2013 and the SOP itself (approved on 4 April 2013) states that several detainees have "*been hunger striking since 2005*" (p1). Therefore, there is a serious risk that Reglan is being administered for longer than the recommended 12-week maximum, increasing the risk of tardive dyskinesia and other side effects beyond any acceptable level.

Increase in risk of side effects

As noted above, side effects of Reglan include tardive dyskinesia, as well as "*[d]epression, thoughts about suicide, and suicide*". The warning label for Reglan states: "*Metoclopramide should be given to patients with a prior history of depression only if the expected benefits outweigh the potential risks*". Given that most detainees at Guantánamo Bay have been held without charge for over 11 years, and have been driven to hunger-strike because they see no hope of release, the potential risks of administering depressive medications within this population are very serious. Several of our clients have recently reported suicidal thoughts or suicide attempts among hunger-striking prisoners.

C. Actions requested

(1) Suspension of approval

We understand that in accordance with 21 CFR 10.30, it is possible that petitioners will not receive a response from you for 180 days. During this period, the continued use of Reglan may cause grave and irreparable damage to detainees' health including the development of tardive dyskinesia, or symptoms of depression. Therefore we would ask that the Commissioner suspends approval of Reglan for use in force-feeding at Guantánamo Bay as a matter of urgency, due to the imminent hazard to the health of affected detainees, pending investigation of the misuse of this drug.

(2) Investigation of adequacy of communication of Medication Guide

In your letter to ANI Pharmaceuticals, Inc. dated 08/02/2011 (the "8 February Letter"), the FDA stated "*We have determined that maintaining the Medication Guide as part of the approved labelling is adequate to address the serious and significant public health concern*".[7] The failure of the SOP to mention the Medication Guide or the side effects of Reglan raises significant concerns as to whether this is being adequately communicated by the manufacturer, as required by 21 CFR 208.24. We therefore ask that the Commissioner investigates whether ANI Pharmaceuticals, Inc. their distributors, packers and/or authorized dispensers are taking adequate steps to ensure Medication Guides are provided to patients at Guantánamo, and takes any appropriate enforcement action arising out of the findings.

(3) Consideration of new REMS requirement

In the 8 February Letter, the FDA released ANI Pharmaceuticals, Inc from the requirement to maintain a REMS in respect of Reglan. Under §355-1 FDCA, a REMS may be required "*to ensure that the benefits of the drug outweigh the risks of the drug*". The evidence of apparent abuse of Reglan at Guantánamo suggests there are serious shortcomings in the current strategy for mitigating the risks of side effects. Therefore, we request that the Commissioner urgently assesses whether a new or revised REMS should be submitted by ANI for Reglan.

[7] Appendix 7.

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III. Environmental impact

There is no environmental impact associated with this petition and we claim a categorical exclusion pursuant to 21 CFR §25.30 and §25.31.

IV. Economic impact

Not applicable at this time.

V. Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which is unfavorable to the petition.

Catherine Gilfedder

Corporate Social Responsibility Advocate

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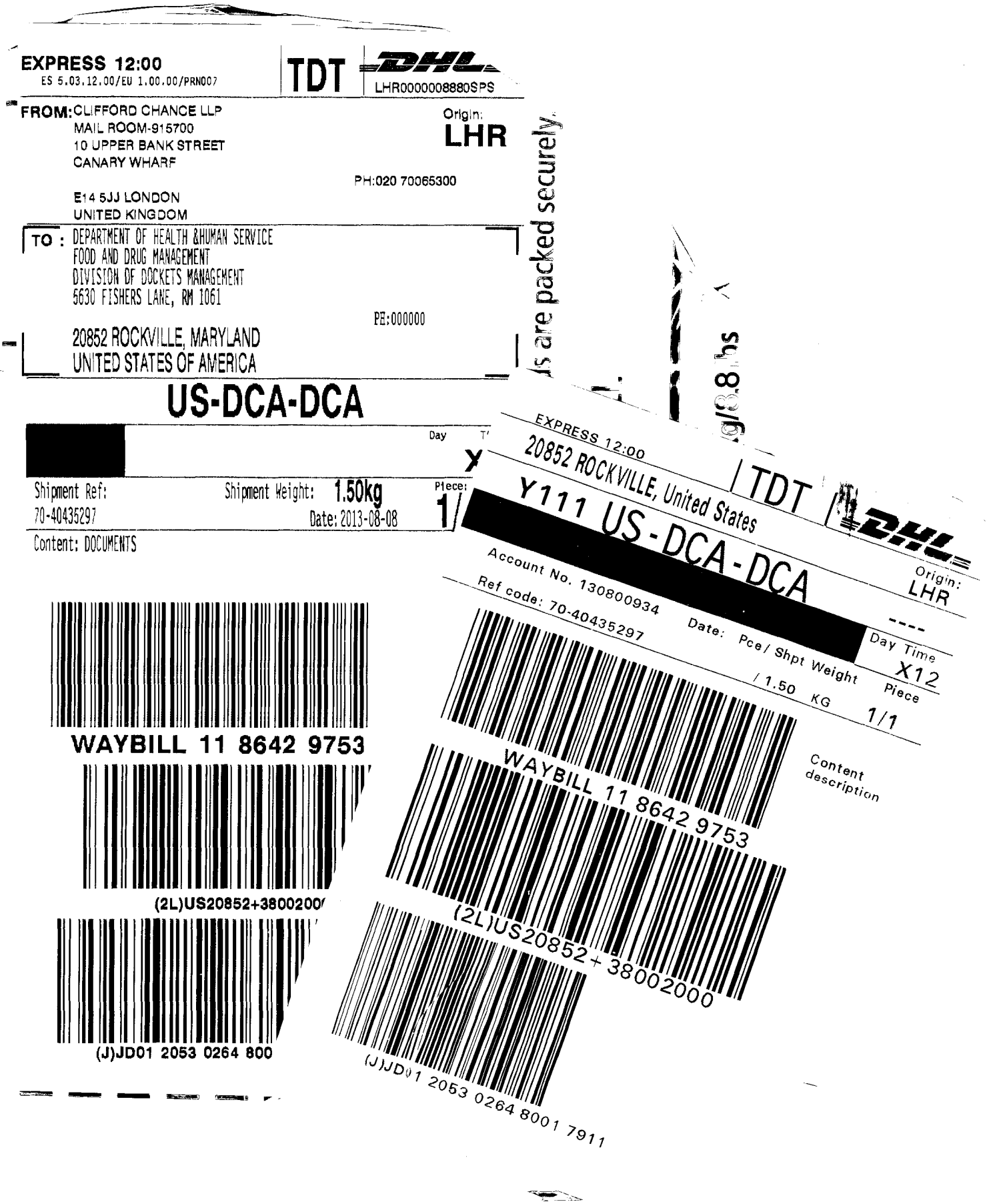

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