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Hepatotoxicity associated with weight loss or sports dietary supplements, including OxyELITE Pro™ — United States, 2013

Kevin Chatham-Stephens,[a,b]* Ethel Taylor,[b] Arthur Chang,[b] Amy Peterson,[c] Johnni Daniel,[b] Colleen Martin,[b] Patricia Deuster,[d] Rebecca Noe,[b] Stephanie Kieszak,[b] Josh Schier,[b] Karl Klontz[e] and Lauren Lewis[b]

In September 2013, the Hawaii Department of Health (HDOH) was notified of seven adults who developed acute hepatitis after taking OxyELITE Pro™, a weight loss and sports dietary supplement. CDC assisted HDOH with their investigation, then conducted case-finding outside of Hawaii with FDA and the Department of Defense (DoD).

We defined cases as acute hepatitis of unknown etiology that occurred from April 1, 2013, through December 5, 2013, following exposure to a weight loss or muscle-building dietary supplement, such as OxyELITE Pro™. We conducted case-finding through multiple sources, including data from poison centers (National Poison Data System [NPDS]) and FDA MedWatch.

We identified 40 case-patients in 23 states and two military bases with acute hepatitis of unknown etiology and exposure to a weight loss or muscle building dietary supplement. Of 35 case-patients who reported their race, 15 (42.9%) reported white and 9 (25.7%) reported Asian. Commonly reported symptoms included jaundice, fatigue, and dark urine. Twenty-five (62.5%) case-patients reported taking OxyELITE Pro™. Of these 25 patients, 17 of 22 (77.3%) with available data were hospitalized and 1 received a liver transplant. NPDS and FDA MedWatch each captured seven (17.5%) case-patients.

Improving the ability to search surveillance systems like NPDS and FDA MedWatch for individual and grouped dietary supplements, as well as coordinating case-finding with DoD, may benefit ongoing surveillance efforts and future outbreak responses involving adverse health effects from dietary supplements. This investigation highlights opportunities and challenges in using multiple sources to identify cases of suspected supplement associated adverse events. Published 2016. This article is a U.S. Government work and is in the public domain in the USA.

Keywords: Supplement; hepatitis; OxyELITE Pro

Introduction

Dietary supplements are commonly used in the United States.[1,2] Some populations, such as military personnel, are more likely to use certain types of dietary supplements, such as weight loss or sports supplements, than the general population.[3] Some of these dietary supplements, particularly herbal products and those used for performance enhancement, have been associated with liver injury.[4–6] No comprehensive surveillance system is available for dietary supplement-induced liver injury, so information regarding supplement induced liver injury comes from case reports and series, outbreak investigations, prospective registries, and voluntary reporting to FDA MedWatch and poison centers.[7]

On September 9, 2013, clinicians at a single tertiary care hospital in Hawaii notified the Hawaii Department of Health (HDOH) of seven patients who presented with severe acute hepatitis and fulminant liver failure of unknown etiology.[8] Abnormal laboratory findings included markedly elevated liver enzymes (aspartate aminotransferase [AST] and alanine aminotransferase [ALT]), as well as total bilirubin. Testing for infectious agents, including hepatitis serologies, was negative; however, clinicians noted that all seven patients consumed OxyELITE Pro™, a weight loss or sports dietary supplement. On September 27, 2013, staff from the U.S. Centers for Disease Control and Prevention (CDC) joined HDOH to assist with their investigation. Case-finding efforts in Hawaii identified 52 case-patients with acute hepatitis of unknown etiology who

* Correspondence to: Kevin Chatham-Stephens, EIS officer, 1600 Clifton Road NE MS C-09 Atlanta, GA 30329 E-mail: xdc4@cdc.gov

a EIS officer, 1600 Clifton Road NE MS C-09, Atlanta, GA

b Division of Environmental Hazards and Health Effects, National Center for Environmental Health, Centers for Disease Control and Prevention

c Division of Integrated Biosurveillance, Armed Forces Health Surveillance Center

d Department of Military and Emergency Medicine, Uniformed Services University

e Office of Analytics and Outreach, Center for Food Safety and Applied Nutrition, Food and Drug Administration

AASLD, — American Association for the Study of Liver Diseases; AFHSC, — Armed Forces Health Surveillance Center; ALT, — Alanine aminotransferase; ANA, — Antinuclear antibody; AST, — Aspartate aminotransferase; BMI, — Body mass index; CDC, — Centers for Disease Control and Prevention; DMSS, — Defense Medical Surveillance System; DoD, — Department of Defense; FDA, — Food and Drug Administration; HDOH, — Hawaii Department of Health; INR, — International normalized ratio; IU/L, — International units per liter; kg/m^2, — Kilogram/meter squared; mg/dL, — Milligram/deciliter; MMWR, — Morbidity and Mortality Weekly Report; NPDS, — National Poison Data System; UNOS, — United Network for Organ Sharing

had ingested a dietary supplement during the 60 days prior to illness onset. These case-patients, the majority of whom consumed OxyELITE Pro™, are described elsewhere.[9]

Based on the preliminary findings from the Hawaii investigation, the U.S. Food and Drug Administration (FDA) initiated an investigation into the manufacture and distribution of OxyELITE Pro™. Case-patients reported using OxyELITE Pro™ products from multiple lots, and a trace back investigation found each of these lots was distributed to states in addition to Hawaii. Due to the nationwide distribution of OxyELITE Pro™, CDC, in collaboration with FDA and U.S. Department of Defense (DoD), initiated case-finding in the United States outside of Hawaii for additional cases of acute hepatitis of unknown etiology and exposure to a weight loss or muscle building dietary supplement. This manuscript describes the different sources through which we identified suspected case-patients and summarizes the presenting signs and symptoms, exposures, and laboratory data from these case-patients.

Methods

We defined a case as acute hepatitis of unknown etiology that developed between April 1, 2013, and December 5, 2013, in a non-Hawaii resident who consumed a dietary supplement marketed for weight loss or muscle building in the 60 days prior to illness onset. Case-patients had 1) an ALT value ≥ four times the upper limit of normal (approximately 160 international units per liter, IU/L); 2) a total bilirubin level ≥ two times the upper limit of normal (approximately 2.5 milligrams per deciliter, mg/dL); 3) a negative viral hepatitis panel; 4) hepatic imaging (i.e., ultrasound, CT scan, MRI) not consistent with alternative etiologies of non-viral hepatitis (e.g., cholelithiasis); 5) no recent hypotensive shock or septic episodes; 6) no pre-existing diagnosis of a chronic liver disease such as autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, Wilson's disease, or hemochromatosis; and 7) no chronic alcohol abuse documented in their medical record. The only difference between our case definition and the one used in the Hawaii investigation was that we restricted our case definition to non-Hawaii residents.[9]

We used four distinct approaches to identify potential cases — National Poison Data System (NPDS), FDA MedWatch, a national call for cases, and DoD case finding. Case-finding from NPDS and FDA MedWatch was restricted to cases involving OxyELITE Pro™. Below are descriptions of the four approaches used.

1. *NPDS* — NPDS collects information from all calls received by U.S. poison centers.[10] When an individual or healthcare provider calls to report an exposure to a product, poison center staff collects information on the exposure and assigns a unique, product-specific numerical code for the exposure. Since dietary supplements are coded individually and no product code encompasses all dietary supplements, we included calls involving only the product code for OxyELITE Pro™. We retrospectively searched NPDS for all calls received between April 1, 2013, and September 25, 2013, in which a caller reported an exposure to OxyELITE Pro™ and had an elevated ALT or total bilirubin. We selected April 1, 2013, based on the earliest exposure among the initial seven patients reported to HDOH. We conducted prospective case-finding from September 30, 2013, through December 5, 2013, at which point we ceased surveillance given the most recent illness onset date of November 3, 2013.
2. *MedWatch* — FDA MedWatch is a system for consumers, patients, and healthcare providers to report adverse events associated with a variety of products, including medications, medical devices, and supplements.[11] FDA searched MedWatch for reports of adverse health effects associated with OxyELITE Pro™ and collected medical records for select patients for which a description of liver disease was provided, along with a history of OxyELITE Pro™ ingestion. For this analysis we included cases reported between April 1, 2013, and December 5, 2013.
3. *National call for cases* — We requested cases through a Health Alert Network advisory distributed to state and local health departments, clinicians, and public health laboratories on October 8, 2013, and a short communication in CDC's Morbidity and Mortality Weekly Report (MMWR) on October 10, 2013.[12,13] The Health Alert Network advisory and MMWR described the preliminary results of the investigation, including that the majority of patients identified had consumed OxyELITE Pro™, and requested that clinicians report patients meeting the case definition to their local or state health department and FDA MedWatch. We also sent a call for cases to the American Association for the Study of Liver Diseases (AASLD) and the United Network for Organ Sharing (UNOS). To facilitate case reports, CDC established a hotline for healthcare providers to report cases of acute hepatitis of unknown etiology associated with consumption of a weight loss or muscle building dietary supplement through December 5, 2013.
4. *DoD case finding* — Given the prevalence of dietary supplement use among active duty military personnel, DoD performed active surveillance for cases by using the Defense Medical Surveillance System (DMSS), which is maintained by the Armed Forces Health Surveillance Center (AFHSC).[14,15] The DMSS was used to identify a cohort of U.S. active duty military personnel and other beneficiaries who had ALT and total bilirubin values consistent with the case definition and had an ICD-9 diagnosis of acute or unspecified hepatitis from April 1, 2013, through December 5, 2013. Potential cases were excluded if they had a diagnosis or laboratory evidence of viral, bacterial, or pre-existing chronic hepatitis. DoD personnel then contacted these individuals to determine whether they had exposure to a dietary supplement marketed for weight loss or muscle building or had any previous medical history that would exclude them as a case. In addition, each service put out a call for cases through their public health centers asking for any case of liver injury without a clear etiology.

Individuals meeting the case definition were administered a questionnaire which focused on demographics; presence and timing of signs and symptoms; previous medical history; any use of prescription drugs, over-the-counter medications, and dietary supplements in the 60 days prior to illness onset; risk factors for liver injury (e.g., Tylenol [acetaminophen] and ethanol use) in the 60 days prior to illness onset; and outcomes including hospitalization, liver transplantation, and death. DoD personnel administered a modified version of the questionnaire that included DoD-specific questions. We standardized race according to U.S. Census categories and categorized case-patients into the following groups — Pacific Islander, Asian, white, multiple races, and other. We asked case-patients specifically about consumption of OxyELITE Pro™ as well as all other supplements. Information on supplement use included supplement name, serving sizes and frequency, dates of use, reasons for use, and locations of purchase. For case-patients with available medical charts, we abstracted results for autoimmune markers and peak laboratory values associated with liver injury. We reviewed case

reports from the different data sources and identified potential duplicate reports based on demographic data. We then compared the data in these potential duplicates, rectified any discrepancies, and confirmed the final data with the state health departments and DoD.

We entered data from the questionnaire and chart abstraction into a Microsoft Excel database and calculated frequencies and proportions of reported values and responses using SAS version 9.3 (SAS Institute, Cary, NC).

Results

Case reporting

We received 86 possible case reports: 40 met the case definition; 27 did not meet the case definition; and 19 did not have enough information to determine their case status. The 40 case-patients lived in 23 states and two military bases outside the United States (Fig. 1). Case-patients were identified through the DoD (n = 21; 52.5%), NPDS (n = 7; 17.5%), FDA MedWatch (n = 7; 17.5%), state or local health departments (n = 3; 7.5%), transplant specialists (n = 1; 2.5%), and the CDC hotline (n = 1; 2.5%). Seven (17.5%) of the 40 case-patients had questionnaire and medical chart data; an additional 30 (75.0%) case-patients had either medical chart or questionnaire data, and three (7.5%) case-patients had basic data collected from the case report form (Table 1).

Demographics and presenting illness

Mean age of the 40 case-patients was 33.9 years, with a range of 20–51 years. Twenty-four (60.0%) of the 40 case-patients were male. Thirty-five of the 40 case-patients reported a race, most commonly white (n = 15; 42.9%), Asian (n = 9; 25.7%), and Pacific Islander (n = 5; 14.3%) (Table 2). The median body mass index (BMI) for the 32 case-patients with available data was 28.0 kg/m^2 (range: 20.6–43.1); 26 (81.3%) case-patients were categorized as overweight or obese. Illness onset dates, which were available for 38 case-patients, ranged from April 10, 2013, through November 3, 2013 (Fig. 2). The most commonly reported signs and symptoms included jaundice or scleral icterus, fatigue, dark urine, nausea, and light- or clay-colored stools (Table 2).

Exposure to OxyELITE Pro™, alcohol, and medications

Twenty-five (62.5%) of 40 case-patients reported consuming OxyELITE Pro™ whereas 15 (37.5%) reported consuming only another dietary supplement in the 60 days prior to illness onset. Of the 25 case-patients who consumed OxyELITE Pro™, nearly half (n = 12; 48%) consumed at least one other supplement, and greater than a quarter (n = 7; 28%) consumed only OxyELITE Pro™ and no other supplements (Table 3). Five of the 6 cases with incomplete information on supplement use were identified through NPDS or FDA MedWatch. No additional supplements were reported in common among the 12 case-patients who consumed OxyELITE Pro™ and another dietary supplement. Of the 15 case-patients who did not consume OxyELITE Pro™, three consumed C4™, two consumed NO-Xplode™, and ten consumed some other weight loss or muscle building supplement. One case-patient who was originally reported to a poison center due to exposure to OxyELITE Pro™ subsequently reported consuming only another dietary supplement instead of OxyELITE Pro™.

Among the 25 case-patients exposed to OxyELITE Pro™, 17 provided a reason for use: 10 (58.8%) to lose weight; four (23.5%) to improve athletic performance; two (11.8%) to increase energy; and one (5.9%) to increase muscle mass. For the 17 case-patients who reported their serving size, all consumed from one to three tablets or scoops per day, which was consistent with manufacturer recommendations. For the 19 case-patients who could remember when they started consuming OxyELITE Pro™, the median duration of OxyELITE Pro™ use prior to illness onset was 55 days (range: 2–477 days).

Twenty-three (71.9%) of 32 case-patients with available data reported drinking any alcohol in the two months before illness onset. Twelve (66.7%) of 18 case-patients reported consuming two or fewer servings of alcohol at each sitting. Of the 12 case-patients who used a prescription or over-the-counter medication in the two months prior to illness onset, two (16.7%) reported taking acetaminophen "a few times a month," and one (8.3%) reported taking ibuprofen "a few times per week."

Figure 1. State of Residence for Case-patients — United States, 2013, n = 40

Table 1. Source of Case Report by Source of Data Collection — United States, 2013

Source	Questionnaire and medical chart	Questionnaire	Medical chart	Case report form	Total
Department of Defense	–	21	–	–	21
Food and Drug Administration MedWatch	1	–	5	1	7
National Poison Data System	2	3	–	2	7
State Health Departments	3	–	–	–	3
Transplant Specialists	1	–	–	–	1
Centers for Disease Control and Prevention Hotline	–	1	–	–	1
Total	7	25	5	3	40

Table 2. Demographics, presenting signs and symptoms, and laboratory tests for case-patients — United States, 2013*

		All case-patients n (%)	Case-patients exposed to OxyELITE Pro™ n (%)
Sex	Male	24 (60.0)	10 (40.0)
	Female	16 (40.0)	15 (60.0)
Race	White	15 (42.9)	4 (20.0)
	Asian	9 (25.7)	9 (45.0)
	Pacific Islander	5 (14.3)	5 (25.0)
	Black	3 (8.6)	0 (0.0)
	Other	2 (5.7)	1 (5.0)
	Multiple races	1 (2.9)	1 (5.0)
Signs and symptoms	Jaundice	29 (90.6)	16 (94.1)
	Fatigue	29 (87.9)	18 (100.0)
	Dark urine	28 (84.9)	17 (94.4)
	Nausea	24 (75.0)	14 (82.4)
	Light- or clay-colored stools	22 (71.0)	13 (81.3)
	Appetite loss	20 (62.5)	14 (82.4)
	Abdominal pain	18 (54.6)	10 (55.6)
Laboratory Test	Reference Range †	Median Value (Range)	Median Value (Range)
AST, IU/L	10–34	1,382 (138–2,525)	1,500 (853–2,525)
ALT, IU/L	10–40	1,597 (391–2,843)	1,849 (975–2,843)
Alkaline phosphatase, IU/L	44–147	166 (115–331)	166 (115–331)
Total bilirubin, mg/dL	0.3–1.9	6.7 (2.4–26.4)	6.1 (2.4–26.4)
INR	0.8–1.1	1.2 (0.8–3.8)	1.2 (1.0–3.8)

* The number of case-patients who responded to each question varied

† Reference ranges obtained from National Library of Medicine

Laboratory Data

Median laboratory values at the peak of illness are presented in Table 2, with markedly elevated AST, ALT, and total bilirubin levels.

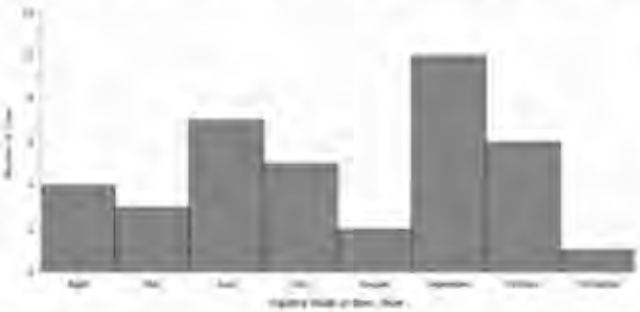


Figure 2. Reported Month of Symptom Onset for Case-patients — United States, 2013, n = 38

Two (25%) of the eight case-patients tested for antinuclear antibody (ANA) had positive tests and one of five (20%) tested for anti-smooth muscle antibody had a positive test. One of three case-patients (33%) tested for F-actin antibody had a positive test and another (33%) had a weakly positive test. One of five (20%) case-patients tested for anti-mitochondrial antibody had positive tests and both case-patients tested for anti-liver kidney microsomal antibody had negative tests. Twelve (63%) of 19 case-patients with available data required a liver biopsy. For the three case-patients with liver biopsy data available, two (67%) had histopathological changes compatible with drug-induced liver injury and autoimmune features and one (33%) case-patient had non-specific findings.

Hospitalization and Outcome

Twenty-six (70.3%) of 37 case-patients with available data and 17 (77.3%) of 22 patients exposed to OxyELITE Pro™ with available data

were hospitalized. Three (27.3%) of 11 case-patients with available data received N-acetylcysteine and four (36.4%) of 11 case-patients with available data received corticosteroids. Of the 25 patients exposed to OxyELITE Pro™, 1 (5.9%) of 17 with available data received a liver transplant. No case-patients died.

Discussion

Forty case-patients, including 25 case-patients who consumed OxyELITE Pro™, in 23 states and two military bases outside the United States developed acute hepatitis between April 1, 2013, and December 5, 2013 following consumption of a weight loss or sports dietary supplement. Viral hepatitis panels were reported to be negative for each case-patient, and case-patients did not report risk factors such as routine acetaminophen use in the 60 days prior to illness onset. This investigation (40 total case-patients; 25 consumed OxyELITE Pro™) and the Hawaii investigation (52 total case-patients; 44 consumed OxyELITE Pro™) identified a combined total of 92 case-patients, of whom 69 consumed OxyELITE Pro™.[9] Of these 69 case-patients who consumed OxyELITE Pro™, 32 required hospitalization, 3 required liver transplants, and 1 died.

Prior to our investigation, FDA had received reports of acute adverse health effects associated with the use of a formulation of OxyELITE Pro™ containing 1,3-dimethylamylamine (DMAA).[16] A study published in 2014 documented acute liver injury in seven active duty service members who had consumed a formulation of OxyELITE Pro™ labeled as containing DMAA.[17] The manufacturer released a DMAA-free formulation of OxyELITE Pro™ that included aegeline in early 2013.[18] After FDA notified the manufacturer that it had failed to inform FDA of the use of aegeline, which was determined to be a new dietary ingredient, the manufacturer recalled aegeline-containing formulations of OxyELITE Pro™ in November 2013.

Dietary supplements and medications associated with liver injury appear to do so through two main mechanisms: either a predictable, dose-dependent toxic effect from a medication (e.g., acetaminophen) or a less predictable, immuno-allergic, idiosyncratic reaction to an ingredient of the product.[19] Although the exact incidence of liver injury associated with dietary supplements is unknown, a prospective study of drug-induced liver injury identified dietary supplements as the cause of liver injury in 130 (15.5%) of 839 consecutively enrolled patients.[5]

Drug- or herb-induced liver injury can be a difficult diagnosis given the absence of safety data on many ingredients contained in these products; the presence of co-exposures potentially associated with liver injury including medications, supplements, and alcohol; interactions among the multiple ingredients in products and drugs; and the lack of a definitive laboratory test for drug-induced liver injury. Although several clinical diagnostic criteria have been published, there is no standardized algorithm to diagnose drug-induced liver injury.[7] Instead, the diagnosis is one of exclusion — it relies on a temporal association of exposure followed by the development of signs and symptoms, and more importantly, the exclusion of other causes of liver injury.[7,20] Therefore, in this investigation we chose a specific case definition to exclude other causes of liver injury such as viral hepatitis; pre-existing autoimmune hepatitis; chronic alcohol use; and chronic liver diseases.

Since dietary supplements often contain multiple ingredients, some with unknown safety profiles and most with unknown interactions, determining the etiologic agent and mechanism of liver injury associated with these products is difficult. A single, definitive etiologic agent is not typically identified in investigations of liver injury associated with a supplement.[21,22] As part of the Hawaii investigation, FDA performed both a general analytic laboratory screen and targeted testing of OxyELITE Pro™ for potentially hepatotoxic agents.[9,16] The testing confirmed the ingredients listed on the label and did not identify any known hepatotoxic agents, so the specific causative ingredient remains unknown. The absence of a known hepatotoxic agent identified on testing may suggest either the presence of a less common hepatotoxic agent that was not tested for, an idiosyncratic reaction to one of the listed ingredients, or a reaction to the combination of ingredients in the product. In addition to the product testing, FDA performed a trace back of OxyELITE Pro™ but did not identify a unique lot common to case-patients in the Hawaii investigation.[9,18] Compared to the Hawaii investigation, where 52 case-patients were identified, we identified 40 case-patients in several states, with California being the only state with more than 3 cases. The reason for this apparent clustering of case-patients in Hawaii without any clustering of case-patients in the continental United States remains unclear.

Our investigation demonstrated characteristics consistent with previous reports of drug-induced liver injury. In a prospective study of 839 consecutively enrolled patients with suspected drug-induced liver injury, 60% of patients were female and the median duration of supplement use was 30 days for non-bodybuilding supplements and 43.5 days for bodybuilding supplements.[5] In our investigation 40% of the patients were female and the median duration of supplement use was 55 days. Similar to our investigation and the investigation in Hawaii, case-patients in some prior investigations of drug- or herb-induced liver injury reported consuming the serving sizes recommended by the manufacturers.[23,24] The increases in ALT, AST, and total bilirubin with only a borderline elevation in alkaline phosphatase observed in our investigation suggest a hepatocellular pattern of liver injury, which is often observed in drug- or herb-induced liver injury.[4,25]

In our study, 25.7% of the 35 individuals with available race data reported Asian as their race compared to 4.8% of the 2010 U.S. population.[26] In a previous study of idiosyncratic drug-induced liver injury, Asians were also over-represented, comprising 6.8% of

Table 3. Case-patients who Reported Consuming OxyELITE Pro™ by Source of Identification and Other Supplement Use — United States, 2013 (n = 25)

	Identified through NPDS or FDA MedWatch n (%)	Identified by DoD, state health department, or CDC Hotline n (%)	Overall n (%)
Consumed only OxyELITE Pro™	3 (23.1)	4 (33.3)	7 (28.0)
Consumed OxyELITE Pro™ and another supplement	5 (38.5)	7 (58.3)	12 (48.0)
Incomplete information on supplement use other than OxyELITE Pro™	5 (38.5)	1 (8.3)	6 (24.0)

the case-patients compared to 3.6% of the 2000 U.S. population.[25] Whether this racial distribution can be attributed to purchasing practices, genetic differences suggesting that Asians may be at higher risk for drug-induced liver injury, cultural practices placing Asians at higher risk for exposure to a hepatotoxic agent, or some other unidentified factor remains unclear. A nationally representative survey documented that individuals from multiple races and Asians had the highest rates of dietary supplement use, with 24.6% of Asians reporting supplement use.[27] In a prospective study of 660 patients diagnosed with drug-induced liver injury by the Drug Induced Liver Injury Network, Asian race was a risk factor for both liver transplantation and death within six months of diagnosis. The reason for this finding is unclear, but the authors postulate that Asians may: 1) have greater susceptibility to drug-induced liver injury, 2) present later in the course of illness; or 3) have impaired liver regeneration.[28]

The significance of the positive autoimmune antibodies in some of our case-patients is also unclear. Prior studies have documented autoimmune antibodies such as ANA in cases of drug-induced liver injury. A prospective, multi-center study in the United States documented that 19 (24%) of 79 case-patients with drug-induced liver injury tested for autoimmune antibodies had positive tests.[25] In addition to drug-induced liver injury, these antibodies have been documented in all-cause liver failure, but have not been associated with a particular toxic etiology. Whether these antibodies serve a role in the immunoallergic pathogenesis underlying the idiosyncratic liver injury or if they are a consequence of the liver injury is uncertain.[25,29]

Since no specific surveillance system for drug-induced liver injury exists, we had to use multiple sources for case ascertainment. Three of these sources (NPDS, MedWatch, and the national call for cases) relied on voluntary reporting of cases. The Institute of Medicine estimates that less than half of all poisonings are reported to poison centers, so reports to poison centers may underestimate the true number of cases.[30] Our approach was subject to several limitations. Due to the lack of more generic codes or product terms, we searched NPDS using only the OxyELITE Pro™ product-specific code and FDA searched MedWatch for cases associated with only OxyELITE Pro™. Therefore, case-finding in NPDS and MedWatch was limited to those persons with exposure to OxyELITE Pro™. This inability to identify cases in NPDS and MedWatch with exposure to dietary supplements other than OxyELITE Pro™ resulted in an over-representation of OxyELITE Pro™ use among cases. The identification of cases associated with other dietary supplements may have yielded additional information regarding risk factors for illness. Since information on dietary supplement product used was self-reported, individuals may have incorrectly identified or may not have remembered the supplement they were taking. We attempted to exclude the major causes of acute hepatitis (e.g., viral hepatitis, acetaminophen) through the case definition, questionnaire, and chart abstraction; however, in many cases, we did not have access to complete medical records which might have provided additional information about the cause of liver injury.

We based our case definition on the moderate severity grade developed by the Drug-Induced Liver Injury Network.[31] The strict case definition likely limited our investigation to those case-patients more severely affected and underestimated the true number of cases. Another factor that potentially resulted in underreporting is that only an estimated 45% of U.S. adults who use dietary supplements report the products to their healthcare provider.[32] Therefore, if a patient presented to a healthcare provider with acute hepatitis of unknown etiology and that provider was unaware of the patient's supplement use, the healthcare provider would be unable to report the patient as a case. Although none of the case-patients reported excessive alcohol or acetaminophen consumption, it cannot be determined as to whether their rates of use may have contributed to liver injury. In addition, the descriptive data in our analysis limited our ability to explore specific risk factors for developing acute hepatitis. The exact number of individuals who consume specific supplements, such as OxyELITE Pro™, and the incidence of supplement-induced liver injury are unknown. As such, we cannot quantify the baseline number of dietary supplement-induced liver injuries in the United States, nor can we determine for certain if the overall number of cases of acute hepatitis identified in this investigation is greater than what would be expected based on background incidence.

We recommend that clinicians and supplement users be aware of the potential for adverse health effects from using such products and report adverse health effects to FDA MedWatch, their local poison center, and/or their local or state department of health. We also recommend healthcare providers ask about supplement use during routine and sick visits, especially when evaluating acute hepatitis. We identified case reports through multiple sources, with NPDS and FDA MedWatch accounting for only 7 (17.5%) case reports each. Improving the ability to search surveillance systems like NPDS and FDA MedWatch for individual and grouped dietary supplements, as well as coordinating case-finding with DoD, may benefit ongoing surveillance efforts and future outbreak responses involving adverse health effects from dietary supplements. Due to the racial distribution observed in the case-finding efforts in Hawaii and in our national case-finding efforts, federal agencies are developing ways to collaborate with their partners to explore many issues, including potential genetic components of drug-induced liver injury.

Conclusion

Through multiple sources, we identified 40 persons within the United States, excluding residents of Hawaii, who developed acute hepatitis between April 1, 2013, and December 5, 2013 after consuming a weight loss or sports supplement. Of the 25 persons who reported consuming OxyELITE Pro™, 17 were hospitalized and 1 required a liver transplantation. No case-patients in our investigation died. Combining our results with the Hawaii investigation, 69 case-patients consumed OxyELITE Pro™, of whom 32 required hospitalization, 3 required liver transplants and 1 died. Given that only approximately one-third of case patients were identified by existing surveillance systems (NPDS and FDA MedWatch), improving the ability of these systems to detect cases associated with individual or groups of dietary supplements may benefit future outbreak investigations. Overall, this investigation highlights opportunities and challenges in using multiple sources to identify cases of suspected supplement associated adverse events. Surveillance and outbreak investigations involving dietary supplements should consider searching multiple data sources, including FDA MedWatch, DoD medical health records, and NPDS, for case reports.

References

[1] R. L. Bailey, J. J. Gahche, C. V. Lentino, J. T. Dwyer, J. S. Engel, P. R. Thomas, J. M. Betz, C. T. Sempos, M. F. Picciano. Dietary supplement use in the United States, 2003–2006. *J. Nutr.* **2011**, *141*, 261.

[2] H. M. Blanck, M. K. Serdula, C. Gillespie, D. A. Galuska, P. A. Sharpe, J. M. Conway, L. K. Khan, B. E. Ainsworth. Use of Nonprescription Dietary Supplements for Weight Loss Is Common among Americans. *J. Am. Diet. Assoc.* **2007**, *107*, 441.

[3] J. J. Knapik, R. A. Steelman, S. S. Hoedebecke, E. K. Farina, K. G. Austin, H. R. Lieberman. A systematic review and meta-analysis on the prevalence of dietary supplement use by military personnel. *BMC Complement. Altern. Med.* **2014**, *14*, 1.

[4] V. J. Navarro. Herbal and dietary supplement hepatotoxicity. *Semin. Liver Dis.* **2009**, *29*, 373.

[5] V. J. Navarro, H. Barnhart, H. L. Bonkovsky, T. Davern, R. J. Fontana, L. Grant, K. R. Reddy, L. B. Seeff, J. Serrano, A. H. Sherker, A. Stolz, J. Talwalkar, M. Vega, R. Vuppalanchi. Liver injury from herbals and dietary supplements in the US Drug Induced Liver Injury Network. *Hepatology.* **2014**, *60*, 1399.

[6] R. Teschke, A. Schwarzenboeck, A. Eickhoff, C. Frenzel, A. Wolff, J. Schulze. Clinical and causality assessment in herbal hepatotoxicity. *Expert Opin. Drug Saf.* **2013**, *12*, 339.

[7] C. Bunchorntavakul, K. R. Reddy. Review article: herbal and dietary supplement hepatotoxicity. *Aliment. Pharmacol. Ther.* **2013**, *37*, 3.

[8] M. M. Roytman, P. Porzgen, C. L. Lee, L. Huddleston, T. T. Kuo, P. Bryant-Greenwood, L. L. Wong, N. Tsai. Outbreak of severe hepatitis linked to weight-loss supplement OxyELITE Pro. *Am. J. Gastroenterol.* **2014**, *109*, 1296.

[9] D. I. Johnston, A. Chang, M. Viray, K. Chatham-Stephens, H. He, E. Taylor, L. L. Wong, J. Schier, C. Martin, D. Fabricant, M. Salter, L. Lewis, S. Y. Park. Hepatotoxicity associated with the dietary supplement OxyELITE Pro™ — Hawaii, 2013. *Drug Test. Anal.* **2016**, *8*(3-4), 319.

[10] J. B. Mowry, D. A. Spyker, L. R. Cantilena, N. Mcmillan, M. Ford. 2013 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 31st Annual Report. *Clin. Toxicol.* **2014**, *52*, 1032.

[11] Food and Drug Administration. MedWatch: the FDA safety information and adverse event reporting program. Available at: http://www.fda.gov/Safety/MedWatch/ [14 May **2014**].

[12] Centers for Disease Control and Prevention. Acute hepatitis and liver failure following the use of a dietary supplement intended for weight loss or muscle building. Available at: http://emergency.cdc.gov/han/han00356.asp [05 May **2014**].

[13] S. Park, M. Viray, D. Johnston, E. Taylor, A. Chang, C. Martin, J. Schier, L. Lewis, K. Levri, K. Chatham-Stephens. Notes from the field: acute hepatitis and liver failure following the use of a dietary supplement intended for weight loss or muscle building — May–October 2013. *MMWR Morb. Mortal. Wkly Rep.* **2013**, *62*, 1.

[14] H. R. Lieberman, T. B. Stavinoha, S. M. McGraw, A. White, L. S. Hadden, B. P. Marriott. Use of dietary supplements among active-duty US Army soldiers. *Am. J. Clin. Nutr.* **2010**, *92*, 985.

[15] M. V. Rubertone, J. F. Brundage. The Defense Medical Surveillance System and the Department of Defense Serum Repository: Glimpses of the Future of Public Health Surveillance. *Am. J. Public Health.* **2002**, *92*, 1900.

[16] Food and Drug Administration. Stimulant Potentially Dangerous to Health, FDA Warns. Available at: http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm347270.htm [12 January **2016**].

[17] S. Foley, E. Butlin, W. Shields, B. Lacey. Experience with OxyELITE Pro and acute liver injury in active duty service members. *Dig. Dis. Sci.* **2014**, *59*, 3117.

[18] K. C. Klontz, H. J. Debeck, P. Leblanc, K. M. Mogen, B. J. Wolpert, J. L. Sabo, M. Salter, S. L. Seelman, S. E. Lance, C. Monahan, D. S. Steigman, K. Gensheimer. The role of adverse event reporting in the FDA response to a multistate outbreak of liver disease associated with a dietary supplement. *Public Health Rep.* **2015**, *130*, 526.

[19] M. P. Holt, C. Ju. Mechanisms of drug-induced liver injury. *AAPS J.* **2006**, *8*, E48.

[20] V. J. Navarro, L. B. Seeff. Liver injury induced by herbal complementary and alternative medicine. *Clin. Liver Dis.* **2013**, *17*, 715.

[21] E. Elinav, G. Pinsker, R. Safadi, O. Pappo, M. Bromberg, E. Anis, L. Keinan-Boker, E. Broide, Z. Ackerman, D. N. Kaluski, B. Lev, D. Shouval. Association between consumption of Herbalife® nutritional supplements and acute hepatotoxicity. *J. Hepatol.* **2007**, *47*, 514.

[22] T. L. Fong, K. C. Klontz, A. Canas-Coto, S. J. Casper, F. A. Durazo, T. J. Davern 2nd, P. Hayashi, W. M. Lee, L. B. Seeff. Hepatotoxicity due to Hydroxycut: a case series. *Am. J. Gastroenterol.* **2010**, *105*, 1561.

[23] M. Adachi, H. Saito, H. Kobayashi, Y. Hirie, S. Kato, M. Yoshioka, H. Ishii. Hepatic injury in 12 patients taking the herbal weight loss aids Chaso or Onshido. *Ann. Intern. Med.* **2003**, *139*, 488.

[24] J. T. Favreau, M. L. Ryu, G. Braunstein, G. Orshansky, S. S. Park, G. L. Coody, L. A. Love, T. L. Fong. Severe hepatotoxicity associated with the dietary supplement LipoKinetix. *Ann. Intern. Med.* **2002**, *136*, 590.

[25] A. Reuben, D. G. Koch, W. M. Lee. Acute Liver Failure Study Group. Drug-induced acute liver failure: results of a U.S. multicenter, prospective study. *Hepatology.* **2010**, *52*, 2065.

[26] K. Humes, N. Jones, R. Ramirez. *Overview of race and Hispanic origin: 2010*, U.S. Census Bureau, Washington, DC, **2011**.

[27] J. Kennedy. Herb and supplement use in the US adult population. *Clin. Ther.* **2005**, *27*, 1847.

[28] R. J. Fontana, P. H. Hayashi, J. Gu, K. R. Reddy, H. Barnhart, P. B. Watkins, J. Serrano, W. M. Lee, N. Chalasani, A. Stolz, T. Davern, J. A. Talwalkar. DILIN Network. Idiosyncratic drug-induced liver injury is associated with substantial morbidity and mortality within 6 months from onset. *Gastroenterology.* **2014**, *147*, 96.

[29] P. S. Leung, L. Rossaro, P. A. Davis, Q. Park, A. Tanaka, K. Kikuchi, H. Miyakawa, G. L. Norman, W. Lee, M. E. Gershwin. Acute Liver Failure Study Group. Antimitochondrial antibodies in acute liver failure: implications for primary biliary cirrhosis. *Hepatology.* **2007**, *46*, 1436.

[30] Institute of Medicine. *Forging a Poison Prevention and Control System*. The National Academies Press, Washington, DC, **2004**.

[31] National Institutes of Health. Severity grading in drug-induced liver injury. Available at: http://livertox.nih.gov/Severity.html [19 June **2014**].

[32] C. H. Wu, C. C. Wang, J. Kennedy. Changes in herb and dietary supplement use in the US adult population: A comparison of the 2002 and 2007 National Health Interview Surveys. *Clin. Ther.* **2011**, *33*, 1749.

4

Begin forwarded message:

From: (b)(6)
Subject: RE: Please contact me!!
Date: August 18, 2015 at 3:15:39 PM EDT
To: (b)(6)

I am in atlanta. (b)(6)

From: (b)(6)
Sent: Tuesday, August 18, 2015 10:01 AM
To: (b)(6)
Subject: Please contact me!!

I need to connect with you ASAP

Thanks

(b)(6)
(b)(6) PhD, MPH, FACSM
Professor and Director
Consortium for Health and Military Performance
A DoD Center of Excellence
Department of Military and Emergency Medicine
Uniformed Services University
4301 Jones Bridge Road
Bethesda, MD 20814
Office (b)(6)
FAX

Begin forwarded message:

From: (b)(6)
Subject: RE: Contact
Date: August 18, 2015 at 3:36:38 PM EDT
To: (b)(6)
(b)(6)

I am happy to assist. Since I no longer represent the DoD I cannot directly provide the names to you but I can help you find the proper CDC and DoD points of contact to assist in your enquiry. I will be in a training all day tomorrow but will be on email Thursday as well.

Best,

(b)(6)

(b)(6)
Centers for Disease Control and Prevention
(b)(6)

From: (b)(6)
Sent: Tuesday, August 18, 2015 3:31 PM
To: (b)(6)
Subject: Contact

(b)(6)
Meet (b)(6) (PH officer with CDC but detailed to DoD previously) – she can assist and give you the contacts for CDC and inform you on how to proceed re case names

Cheers

(b)(6)
(b)(6) PhD, MPH, FACSM
Professor and Director
Consortium for Health and Military Performance
A DoD Center of Excellence
Department of Military and Emergency Medicine
Uniformed Services University
4301 Jones Bridge Road
Bethesda, MD 20814
Office (b)(6)
FAX

Begin forwarded message:

From: (b)(6)
Subject: RE: Case Control Study
Date: November 15, 2013 at 4:32:38 PM EST
To: (b)(6)
Cc:
(b)(6) (b)(6)

My BB is below and will be enabled for use in Korea. I will be back 9 am next Friday so will plan on calling in from home, although I will be jet-lagged severely!

Dr. (b)(6) s my back-up, his contact information is: Dr. (b)(6)
(b)(6) (b)(6) BB: (b)(6)
Dr. (b)(6) can be reached at: (b)(6) I am cc'ing her here as well.

(b)(6) PhD. MPH. FACSM
Professor and Director
Consortium for Health and Military Performance
A DoD Center of Excellence
Department of Military and Emergency Medicine
USUHS
4301 Jones Bridge Road
Bethesda, MD 20814
(b)(6)

Office (b)(6)
FAX (b)(6)

(b)(6) DVM, PhD, DACVPM
LCDR USPHS
CDC Guest Researcher
Division of Integrated Biosurveillance (DIB)
Armed Forces Health Surveillance Center (AFHSC)
(b)(6)

From: (b)(6)
Sent: Friday, November 15, 2013 1:24 PM
To: (b)(6)
Cc: (b)(6)
(b)(6)
Subject: Case Control Study

H (b)(6)
I just heard you say on the call that we will be receiving 13 records today. That is very good news. The study seems to be progressing very nicely. You should know that Dr (b)(6) and the CDC OD continue to have intense interest in this outbreak. They are particularly interested in a potential case-control study with DoD. I have explained to the OD that we are focused on the descriptive data for now which will inform the case control. However, I continue to get questions on case/control plans. Thus I think it is a good idea to have a contact while you are in Korea in case we get questions from Dr (b)(6) CDC leadership. Would (b)(6) be the appropriate contact. Is it ok to reach out to (b)(6) next week if needed? Do we have contact info?

Safe travels and thank you,
Lauren

(b)(6)
CAPT, USPHS
Chief, Health Studies Branch
(b)(6)

5

From: [redacted]
To: [redacted]
Cc: [redacted]
Subject: Emails
Date: Wednesday, December 07, 2016 8:48:27 PM

More emails

Begin forwarded message:

From: (b)(6) (b) [redacted]
Subject: RE: Manuscript question
Date: September 15, 2015 at 10:43:53 AM EDT
To: (b)(6) [redacted]

I will look through it and check with Angie at AFHSC

-----Original Message-----
From: (b)(6) (b)(6) [redacted]
Sent: Sunday, September 13, 2015 8:06 PM
To: (b)(6) [redacted]
Cc: [redacted]
(b)(6) [redacted]
Subject: Re: Manuscript question

(b)(6) [redacted]

Where are we? I sent you an draft and have not heard back. What I do know is that the manuscript needs work — I did a thorough edit but could do much more in terms of organizing et al.

Pelase let me know
Thanks
(b)([redacted]

(b)(6) [redacted] PhD, MPH, FACSM
Professor and Director
Consortium for Health and Military Performance A DoD Center of Excellence
Department of Military and Emergency Medicine Uniformed Services University
4301 Jones Bridge Road
Bethesda, MD 20814
Office (b)(6) [redacted]
FAX [redacted]

On Aug 18, 2015, at 5:48 PM, (b)(6) (b)([redacted]
(b)(6) [redacted] wrote:

this will need to go through DoD clearance. The key folks at AFHSC are me and Dr. (b)(6) [redacted] As well, you Dr. (b)(6) [redacted] should be

included in the process. Possibly key folks at the Service public health centers but many folks have moved on in positions so i am not sure how much return we'd get on that.

Best,

(b)(6)

From: (b)(6)
Sent: Tuesday, August 18, 2015 5:42 PM
To: (b)(6)
Cc:
Subject: Re: Manuscript question

(b)(6)

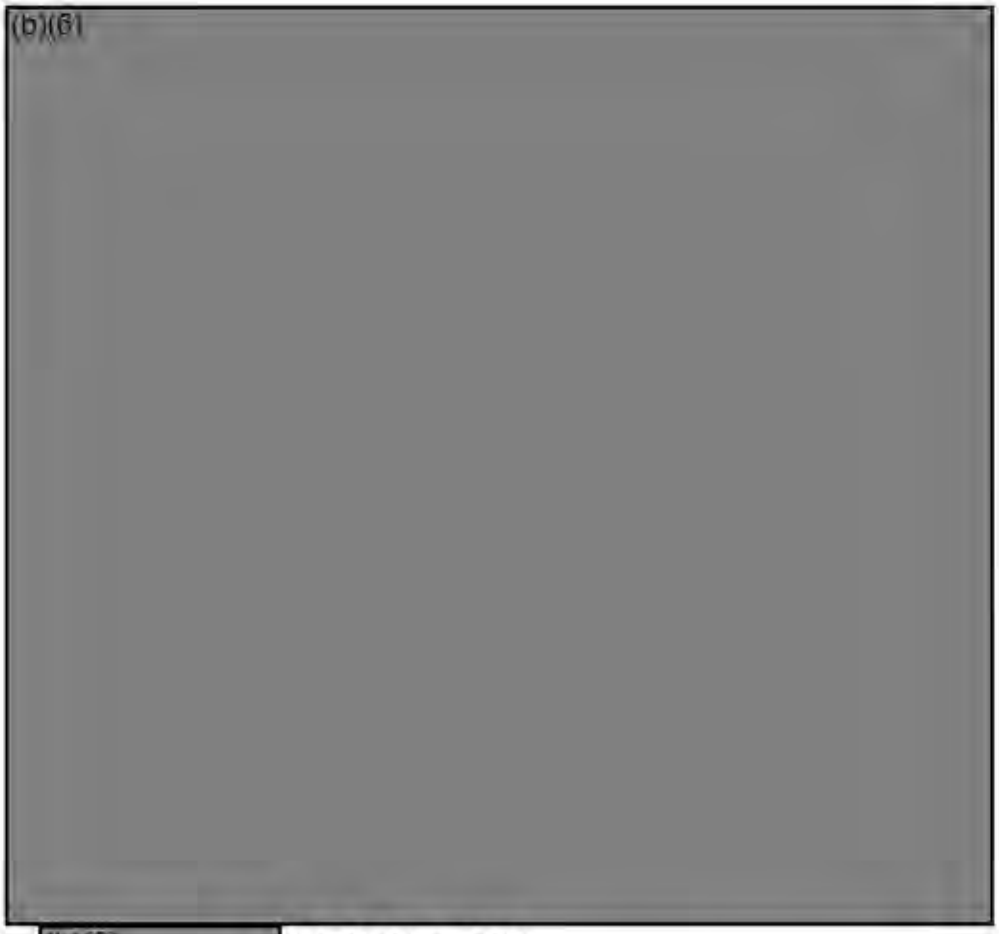
I am pasting the list of those who were actively involved in the effort below -- I am not sure who from DoD was most active, but we had a number of "players"
(b)(-- what are your recollections?

I have not read the manuscript carefully but I believe (b)(can correct me) but DoD also did a call out to all the services for cases so it was not just thru AFHSC -- Also, interesting that the case number dropped as in DoD was had 26 active duty and 5 dependents. I have no intel on Reserves or Guard.

My cursory review suggests it needs some polishing and editing before publishing. Has it been cleared thru DoD?
I also do not see any disclaimers or the like

Standing by to assist
(b)(

From: (b)(6)
Subject: CDC/FDA/DOD Hepatotoxity/Supplement Use Update Call
Date: November 7, 2013 4:56:24 PM EST
To: (b)(6)
(b)(6)



(b)(6) PhD, MPH, FACSM
Professor and Director
Consortium for Health and Military Performance A DoD Center of Excellence Department of Military and Emergency Medicine
Uniformed
Services University
4301 Jones Bridge Road
Bethesda, MD 20814
Office (b)(6)
FAX

On Aug 18, 2015, at 4:38 PM, (b)(6) (b)(6) wrote:

Good afternoon Dr. (b)(6) we're by no means trying to exclude any other partners from this manuscript. When we initially submitted the manuscript to the journal, it did not include any DoD data, so the co-authors included colleagues from CDC and FDA. When the journal asked that we include the DoD data, we communicated this request to (b)(Upon inclusion of the DoD data, we added (b)(as a co-author since she was involved in the outbreak. If there are other co-authors who should be added, then please let me know. We're definitely interested in anything that would make this a stronger and more

cohesive paper.

Please let me know if you would prefer to chat about this. I appreciate your help!

V/R
(b)(

(b)((b)(6) MD, MPH
LCDR U.S. Public Health Service
Medical Officer
Enteric Diseases Epidemiology Branch
National Center for Emerging and Zoonotic Infectious Diseases
Centers
for Disease Control and Prevention Office Phone: (b)(6)
BlackBerry: (b)(6)

-----Original Message-----
From: (b)(6)
Sent: Tuesday, August 18, 2015 4:16 PM
To: (b)(6)
(b)(6)
Cc: (b)(6)
(b)(6)
Subject: Re: Manuscript question

I do not see how you can add DoD data to this with no one from DoD on the paper -- Not sure how to respond -- as clearly it would be a stronger and more cohesive paper, but it is now CDC.

Let me know what you want me to do

V/R
(b)(

(b)(6) PhD, MPH, FACSM
Professor and Director
Consortium for Health and Military Performance A DoD Center of Excellence Department of Military and Emergency Medicine
Uniformed
Services University
4301 Jones Bridge Road
Bethesda, MD 20814
Office (b)(6)
FAX

On Aug 18, 2015, at 4:03 PM, (b)(6) (b)(
(b)(6) wrote:

Hi (b)(here is the version I sent you on 8/6. The journal (Drug Testing & Analysis) requested that we resubmit the manuscript by early September. Please let me know if you have any questions.

Thanks!
(b)(6)

(b)((b)(6) MD, MPH
LCDR U.S. Public Health Service
Medical Officer
Enteric Diseases Epidemiology Branch
National Center for Emerging and Zoonotic Infectious Diseases
Centers
for Disease Control and Prevention Office Phone: (b)(6)
BlackBerry: (b)(6)

-----Original Message-----
From: (b)(6) (b)((b)(6)
Sent: Tuesday, August 18, 2015 3:43 PM
To: (b)(6) (b)((b)(6)
(b)(6) (b)((b)(6)
(b)(6)
Cc: (b)(6) (b)(6) (b)(6)
Subject: RE: Manuscript question

Can you resend the manuscript to me and cc (b)(6) ?

I want her input asap as well.

-----Original Message-----
From: (b)(6) (b)(6)
Sent: Friday, July 10, 2015 10:09 AM
To: (b)(6))(6)
Cc: (b)(6) (b)(6) (b)(6)
Subject: RE: Manuscript question

Hi (b)(we definitely don't want to hijack your data if you're already working on a manuscript! But if you all don't foresee publishing the data, then it seems like it would be beneficial to include the DoD data in the national case-finding manuscript. I think the dietary supplement field is one field where any additional data will hopefully increase awareness, provide additional context to the issue, etc.

Let me know what you think. Thanks!
(b)(6)

(b)((b)(6) MD, MPH
LCDR U.S. Public Health Service
Medical Officer
Enteric Diseases Epidemiology Branch

National Center for Emerging and Zoonotic Infectious Diseases
Centers
for Disease Control and Prevention Office Phone: (b)(6)
BlackBerry: (b)(6)

-----Original Message-----
From: (b)(P (b)(6)
Sent: Friday, July 10, 2015 8:17 AM
To: (b)(6) (b)((b)(6)
Cc: (b)(6) (b)((b)(6)
Subject: Re: Manuscript question

happy to either finish the damn paper or include the data in your paper... i am in the midst of trainings and fiscal year hell but otherwise home still we don't move for awhile yet.

What do you think makes the most sense?

best,

(b)(

On Thu, Jul 9, 2015 at 4:55 PM, (b)(6) (b)((b)(6) wrote:

> Hi (b)(I received the dietary supplement manuscript back as a revise
> and resubmit. I think the biggest issue (noted by 1 reviewer and the
> editor) was the absence of the DoD case-patients. Here are some of the comments:
>
> 1. The rationale for excluding active duty military personnel seems
> weak.
>
> 2. The rationale for excluding active duty personnel does not seem to
> make sense. Other people included in the analysis might have very
> wide-ranging activity levels as well. Was this a logistical issue?
> Did the DoD not share that data or wish to publish separately?
> Regardless the specific reason, even if it's logistical, should be
> described. In addition, if the authors are aware of where this data

is or where it will be published that should be included in the Discussion.

Do you know if DoD is pursuing a manuscript? If not, then how do you
think they'd feel about us including the data from the DoD
case-patients? It would be relatively easy to rerun the same analysis
and present the data in aggregate. Thoughts?

Sorry to keep pestering you about this manuscript!

Where are you these days? Have you already moved?

Thanks!

(b)(6)

(b)(6) MD, MPH

LCDR U.S. Public Health Service

Medical Officer

Enteric Diseases Epidemiology Branch

National Center for Emerging and Zoonotic Infectious Diseases

Centers for Disease Control and Prevention

Office Phone: (b)(6)

BlackBerry: (b)(6)

<Outbreak of Dietary Supplement-Associated Acute Hepatitis_Aug 5_Clean.docx>

Begin forwarded message:

From: (b)(6)
Subject: RE: OEP update
Date: November 24, 2015 at 10:00:34 AM EST
To: (b)(6)
(b)(6)
Cc: (b)(6)

Since I am not going home for the holidays I am relatively free to work on this (other than travel the better part of the next two weeks – the week of the 7th I will be in western province doing site visits)

But we might see lions and elephants on the 8 hr drive out there...

(b)(6) DVM, PhD
Team Lead, Epi and Strategic Info Branch
Centers for Disease Control and Prevention – Zambia
Phone: (b)(6)
Mobile

From: (b)(6)
Sent: Tuesday, November 24, 2015 4:59 PM
To (b)(6)
(b)(6)
Cc: (b)(6)
Subject: FW: OEP update

Dear all,

Apologies for dropping out of this process. I've had a ton of travel and trouble-shooting since arriving here and am just getting comfortable with what my team is doing as we head into field tests for the upcoming national level survey roll- out.

(b)(6) was in touch with me last week to confirm our numbers from the active duty cases for the manuscript and they want to try to get it into the supplement issue. What do we need to do to clear this manuscript with DoD and how should we best proceed?

We also need to finalize our author list for CDC.

Best,

(b)(6)

(b)(6) DVM, PhD
Team Lead, Epi and Strategic Info Branch
Centers for Disease Control and Prevention – Zambia
Phone: (b)(6)
Mobile

From (b)(6)
Sent: Tuesday, November 24, 2015 4:55 PM
To: (b)(6)
Cc:
Subject: OEP update

Hi (b)(6)

Thanks again for going over the OEP numbers with me on Friday. I talked with (b)(6) and we were correct—given our determination that DOD006 is a case and that DOD should NOT be counted as an OEP user, we will be updating the OEP manuscript shortly with a grand total of 92 cases, 69 of whom used OEP, 45 who were hospitalized, and 3 that were transplanted.

Since we are using DOD data now in the paper, do we need to plan to add any additional co-authors from DOD? And do you know what still needs to be done to clear the manuscript as far as DOD is concerned? To get it into the Drug Testing & Analysis supplement we have to have it submitted by Dec. 7 so we are trying to figure out how much time DOD needs on their end.

Thanks for any help you can provide!!!

(b)(6)
DVM, MPH
CDR, US Public Health Service
Health Studies Branch
National Center for Environmental Health
Centers for Disease Control and Prevention
4770 Buford Highway, MS F-60
Chamblee, GA 30341
(o) (b)(6)
(bb) (b)(6)
(f) (b)(6)
(b)(6)

Begin forwarded message:

From: (b)(6)
Subject: RE: Manuscript question
Date: August 18, 2015 at 4:04:36 PM EDT
To: (b)(6)
(b)(6)
Cc: (b)(6)

Thank you!

Best,

(b)(

-----Original Message-----
From: (b)(6)
Sent: Tuesday, August 18, 2015 4:04 PM
To: (b)(6)
(b)(6)
Cc: (b)(6)
Subject: RE: Manuscript question

Hi (b)(here is the version I sent you on 8/6. The journal (Drug Testing & Analysis) requested that we resubmit the manuscript by early September. Please let me know if you have any questions.

Thanks!
(b)(6)

(b)((b)(6) MD, MPH
LCDR U.S. Public Health Service
Medical Officer
Enteric Diseases Epidemiology Branch
National Center for Emerging and Zoonotic Infectious Diseases Centers for Disease Control and Prevention Office Phone: (b)(6)
BlackBerry: (b)(6)

-----Original Message-----
From: (b)(6) (b)((b)(6)
Sent: Tuesday, August 18, 2015 3:43 PM
To: (b)(6)
(b)(6)
Cc: (b)(6) (b)(6) (b)(6)
Subject: RE: Manuscript question

Can you resend the manuscript to me and cc (b)((b)(6)

I want her input asap as well.

-----Original Message-----

From: (b)(6)
Sent: Friday, July 10, 2015 10:09 AM
To: (b)(6)
Cc:
Subject: RE: Manuscript question

Hi (b)(we definitely don't want to hijack your data if you're already working on a manuscript! But if you all don't foresee publishing the data, then it seems like it would be beneficial to include the DoD data in the national case-finding manuscript. I think the dietary supplement field is one field where any additional data will hopefully increase awareness, provide additional context to the issue, etc.

Let me know what you think. Thanks!
(b)(6)

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From: (b)(6)
Sent: Friday, July 10, 2015 8:17 AM
To: (b)(6)
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Subject: Re: Manuscript question

happy to either finish the damn paper or include the data in your paper… i am in the midst of trainings and fiscal year hell but otherwise home still we don't move for awhile yet.

What do you think makes the most sense?

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On Thu, Jul 9, 2015 at 4:55 PM, (b)(6) (b)((b)(6) wrote:

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> and resubmit. I think the biggest issue (noted by 1 reviewer and the editor) was the absence of the DoD case-patients. Here are some of the comments:

1. The rationale for excluding active duty military personnel seems
weak.

2. The rationale for excluding active duty personnel does not seem to
make sense. Other people included in the analysis might have very wide-ranging activity levels as well. Was this a logistical issue? Did the DoD not share that data or wish to publish separately? Regardless

the specific reason, even if it's logistical, should be described. In addition, if the authors are aware of where this data is or where it will be published that should be included in the Discussion.

Do you know if DoD is pursuing a manuscript? If not, then how do you
think they'd feel about us including the data from the DoD case-patients? It would be relatively easy to rerun the same analysis and present the data in aggregate. Thoughts?

Sorry to keep pestering you about this manuscript!

Where are you these days? Have you already moved?

Thanks!

(b)(6)

(b)((b)(6) MD, MPH

LCDR U.S. Public Health Service

Medical Officer

Enteric Diseases Epidemiology Branch

National Center for Emerging and Zoonotic Infectious Diseases

Centers for Disease Control and Prevention

Office Phone: (b)(6)

BlackBerry: (b)(6)

Begin forwarded message:

From: (b)(6)
Subject: Automatic reply: OEP update
Date: November 30, 2015 at 12:23:19 PM EST
To: (b)(6)

I will be out of the office this week. I will have limited access to email but may not be able to reply immediately.

Begin forwarded message:

From: (b)(6)
Subject: RE: Manuscript question
Date: August 18, 2015 at 5:48:44 PM EDT
To: (b)(6)
(b)(6)
Cc: (b)(6)

this will need to go through DoD clearance. The key folks at AFHSC are me and Dr. (b)(6) As well, you Dr. (b)(6) should be included in the process. Possibly key folks at the Service public health centers but many folks have moved on in positions so i am not sure how much return we'd get on that.

Best,

(b)(6)

From: (b)(6)
Sent: Tuesday, August 18, 2015 5:42 PM
To: (b)(6)
Cc:
Subject: Re: Manuscript question

(b)(6)

I am pasting the list of those who were actively involved in the effort below -- I am not sure who from DoD was most active, but we had a number of "players" (b)(6) -- what are your recollections?

I have not read the manuscript carefully but I believe (b)(6) can correct me) but DoD also did a call out to all the services for cases so it was not just thru AFHSC

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Also, interesting that the case number dropped as in DoD was had 26 active duty and 5 dependents. I have no intel on Reserves or Guard.

My cursory review suggests it needs some polishing and editing before publishing. Has it been cleared thru DoD?
I also do not see any disclaimers or the like

Standing by to assist
(b)(

From: (b)(6)
Subject: CDC/FDA/DOD Hepatotoxity/Supplement Use Update Call
Date: November 7, 2013 4:56:24 PM EST
To: (b)(6)
(b)(6)

(b)(6) PhD, MPH, FACSM
Professor and Director
Consortium for Health and Military Performance
A DoD Center of Excellence

Department of Military and Emergency Medicine
Uniformed Services University
4301 Jones Bridge Road
Bethesda, MD 20814
Office (b)(6)
FAX (b)(6)

On Aug 18, 2015, at 4:38 PM, (b)(6) wrote:

Good afternoon Dr. (b)(6) we're by no means trying to exclude any other partners from this manuscript. When we initially submitted the manuscript to the journal, it did not include any DoD data, so the co-authors included colleagues from CDC and FDA. When the journal asked that we include the DoD data, we communicated this request to (b)(Upon inclusion of the DoD data, we added (b)(as a co-author since she was involved in the outbreak. If there are other co-authors who should be added, then please let me know. We're definitely interested in anything that would make this a stronger and more cohesive paper.

Please let me know if you would prefer to chat about this. I appreciate your help!

V/R
(b)(

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Medical Officer
Enteric Diseases Epidemiology Branch
National Center for Emerging and Zoonotic Infectious Diseases
Centers for Disease Control and Prevention
Office Phone: (b)(6)
BlackBerry: (b)(6)

-----Original Message-----
From: (b)(6)
Sent: Tuesday, August 18, 2015 4:16 PM
To: (b)(6)
Cc:
(b)(6)
Subject: Re: Manuscript question

I do not see how you can add DoD data to this with no one from DoD on the paper -- Not sure how to respond -- as clearly it would be a stronger and more cohesive paper, but it is now CDC.

Let me know what you want me to do

V/R
(b)(

(b)(6) (b)(6) PhD, MPH, FACSM
Professor and Director
Consortium for Health and Military Performance A DoD Center of Excellence
Department of Military and Emergency Medicine Uniformed Services University
4301 Jones Bridge Road
Bethesda, MD 20814
Office (b)(6)
FAX (b)(6)

On Aug 18, 2015, at 4:03 PM, (b)(6)
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Hi (b)(here is the version I sent you on 8/6. The journal (Drug Testing & Analysis) requested that we resubmit the manuscript by early September. Please let me know if you have any questions.

Thanks!
(b)(6)

(b)((b)(6) MD, MPH
LCDR U.S. Public Health Service
Medical Officer
Enteric Diseases Epidemiology Branch
National Center for Emerging and Zoonotic Infectious Diseases Centers for Disease Control and Prevention Office Phone: (b)(6)
BlackBerry: (b)(6)

-----Original Message-----
From: (b)(6) (b)((CDC/CGH/DGHA)
Sent: Tuesday, August 18, 2015 3:43 PM
To: (b)(6)
(b)(6)
Cc: (b)(6) (b)(6) (b)(6)
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Medical Officer
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National Center for Emerging and Zoonotic Infectious Diseases Centers for Disease Control and Prevention Office Phone: (b)(6)
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-----Original Message-----
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(b)((b)(6) MD, MPH

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Medical Officer

Enteric Diseases Epidemiology Branch

National Center for Emerging and Zoonotic Infectious Diseases

Centers for Disease Control and Prevention

Office Phone: (b)(6)

BlackBerry: (b)(6)

<Outbreak of Dietary Supplement-Associated Acute Hepatitis_Aug 5_Clean.docx>

Begin forwarded message:

From: (b)(6)
Subject: FW: OEP update
Date: November 24, 2015 at 9:59:19 AM EST
To: (b)(6)
(b)(6)
Cc: (b)(6)

Dear all,

Apologies for dropping out of this process. I've had a ton of travel and trouble-shooting since arriving here and am just getting comfortable with what my team is doing as we head into field tests for the upcoming national level survey roll- out.

(b)(6) was in touch with me last week to confirm our numbers from the active duty cases for the manuscript and they want to try to get it into the supplement issue. What do we need to do to clear this manuscript with DoD and how should we best proceed?

We also need to finalize our author list for CDC.

Best,

(b)(6)

(b)(6) E. (b)(6) DVM, PhD
Team Lead, Epi and Strategic Info Branch
Centers for Disease Control and Prevention – Zambia
Phone: (b)(6)
Mobile

From: (b)(6)
Sent: Tuesday, November 24, 2015 4:55 PM
To: (b)(6)
Cc:
Subject: OEP update

HI (b)(6)

Thanks again for going over the OEP numbers with me on Friday. I talked with (b)(6) and we were correct—given our determination that DOD006 is a case and that DOD should NOT be counted as an OEP user, we will be updating the OEP manuscript shortly with a grand total of 92 cases, 69 of whom used OEP, 45 who were hospitalized, and 3

that were transplanted.

Since we are using DOD data now in the paper, do we need to plan to add any additional co-authors from DOD? And do you know what still needs to be done to clear the manuscript as far as DOD is concerned? To get it into the Drug Testing & Analysis supplement we have to have it submitted by Dec. 7 so we are trying to figure out how much time DOD needs on their end.

Thanks for any help you can provide!!!

(b)(6)
DVM, MPH
CDR, US Public Health Service
Health Studies Branch
National Center for Environmental Health
Centers for Disease Control and Prevention
4770 Buford Highway, MS F-60
Chamblee, GA 30341
(o) (b)(6)
(bb) (b)(6)
(f) (b)(6)
(b)(6)

Begin forwarded message:

From: (b)(6)
Subject: Re: Manuscript question
Date: October 9, 2015 at 4:12:52 AM EDT
To: (b)(6)
(b)(6)

Just arrived Sunday and got connected. I will try to link everyone back up and see where we are. Thanks for the prompt!

Sent from my BlackBerry 10 smartphone.

From: (b)((b)(6)
Sent: Friday, October 9, 2015 3:55 AM
To: (b)(6)
Cc:
Subject: Fwd: Manuscript question

I have yet to hear from you —

(b)((b)(6)

(b)(6) (b)(6) PhD, MPH, FACSM
Professor and Director
Consortium for Health and Military Performance
A DoD Center of Excellence
Department of Military and Emergency Medicine
Uniformed Services University
4301 Jones Bridge Road
Bethesda, MD 20814
Office (b)(6)
FAX (b)(6)

Begin forwarded message:

From: (b)(6) (b)(6) (b)(6)
Subject: Fwd: Manuscript question
Date: September 15, 2015 at 10:45:58 AM EDT
To: (b)(6)
(b)(6)

Dr. (b)(6)
Given (b)(is likely on her honeymoon, I am resending this to you.
Please advise

V/r

(b)(
(b)(6) (b)(6) PhD, MPH, FACSM
Professor and Director
Consortium for Health and Military Performance
A DoD Center of Excellence
Department of Military and Emergency Medicine
Uniformed Services University
4301 Jones Bridge Road
Bethesda, MD 20814
Office (b)(6)
FAX (b)(6)

Begin forwarded message:

From: (b)(6) (b)(6) (b)(6)
Subject: Re: Manuscript question
Date: September 4, 2015 9:52:40 PM EDT
To: (b)(P (b)(6)
Cc: (b)(6)
(b)(6)

(b)(

Here are my comments - which are many and try to bring the literature up to date. Referencing 2002 for supplement use is not appropriate. Also we have included prevalence of use of other DS.

Please let me know how to proceed as this should be reviewed by HA/DHA

Thanks

(b)(

(b)(6) (b)(6) PhD, MPH, FACSM
Professor and Director
Consortium for Health and Military Performance
A DoD Center of Excellence
Department of Military and Emergency Medicine
Uniformed Services University
4301 Jones Bridge Road
Bethesda, MD 20814
Office (b)(6)
FAX (b)(6)

> On Sep 3, 2015, at 8:37 PM, (b)(6) (b)(6) (b)(6) wrote:
>
> (b)(
>
> I am working my way through and should have by Monday or Tuesday. The introduction is very old WRT refs and data - we need to up to date on US andt DoD so am revising that. had many "must dos" but can get to tomorrow and weekend
>
> This needs to go thru DoD MHS and I can send thru USU — who can get approval from HA.
>
> If CDR (b)(6) does not like edits, it needs to take DoD data out as currently the manuscript is clearly lacking knowledge of DoD issues.
>
> V/R
>
> (b)(

(b)(6) (b)(6) PhD, MPH, FACSM

Professor and Director

Consortium for Health and Military Performance

A DoD Center of Excellence

Department of Military and Emergency Medicine

Uniformed Services University

4301 Jones Bridge Road

Bethesda, MD 20814

Office (b)(6)

FAX (b)(6)

> On Aug 31, 2015, at 12:48 PM, (b)(P (b)(6) wrote:
>
> Any suggested edits send to (b)(and myself for collation at this
>
> point, i will work with them.
>
> Best,
>
> (b)(
>
> On Mon, Aug 31, 2015 at 12:34 PM, (b)(6) (b)(6)
>
> (b)(6) wrote:
>
> > I have not started edits as I was not clear as to what is wanted. I know my initial read suggested it needs a good edit

I will wait for (b)(to respond.

Hope all is well.

V/R

(b)(

(b)(6) (b)(6) PhD, MPH, FACSM

Professor and Director

Consortium for Health and Military Performance

A DoD Center of Excellence

Department of Military and Emergency Medicine

Uniformed Services University

4301 Jones Bridge Road

Bethesda, MD 20814

Office (b)(6)

FAX (b)(6)

On Aug 31, 2015, at 12:03 PM, (b)(6) (b)((b)(6) wrote:

Hello Dr. (b)(6) I was out on

family matters at the end of last week, so my apologies for the delay in responding. I believe Dr. (b)(6) and (b)(are both in the process of reviewing the manuscript. Since I'm an outsider, I'll need to defer to you, (b)(and Dr. (b) on the best next steps for the manuscript. If you have reviewed the manuscript and have edits/comments/etc., then please forward those to me and (b)(If there are other actions that need to be taken, then please send them to (b)(and me as well.

Thanks!

(b)(6)

(b)((b)(6) MD, MPH

LCDR U.S. Public Health Service

Medical Officer

Enteric Diseases Epidemiology Branch

National Center for Emerging and Zoonotic Infectious Diseases

Centers for Disease Control and Prevention

Office Phone: (b)(6)

BlackBerry: (b)(6)

-----Original Message-----

From: (b)(6) (b)(6)
(b)(6)

Sent: Thursday, August 27, 2015 9:11 PM

To: (b)(6) (b)(6)
(b)(6)
(b)(6)

Cc: (b)(6) (b)(6)
(b)(6)
(b)(6)

Subject: Re: Manuscript question

CDR (b)(6)

Please let me know what you would like to do.

V/R

(b)(6)

(b)(6) (b)(6) PhD, MPH, FACSM

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Bethesda, MD 20814

Office (b)(6)

FAX (b)(6)

On Aug 18, 2015, at 5:42 PM, (b)(6) (b)(6) (b)(6) (b)(6) wrote:

(b)(6)

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I also do not see any disclaimers or the like

Standing by to assist

(b)(

From: (b)(6)
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Subject: CDC/FDA/DOD Hepatotoxity/Supplement Use Update Call

Date: November 7, 2013 4:56:24 PM EST

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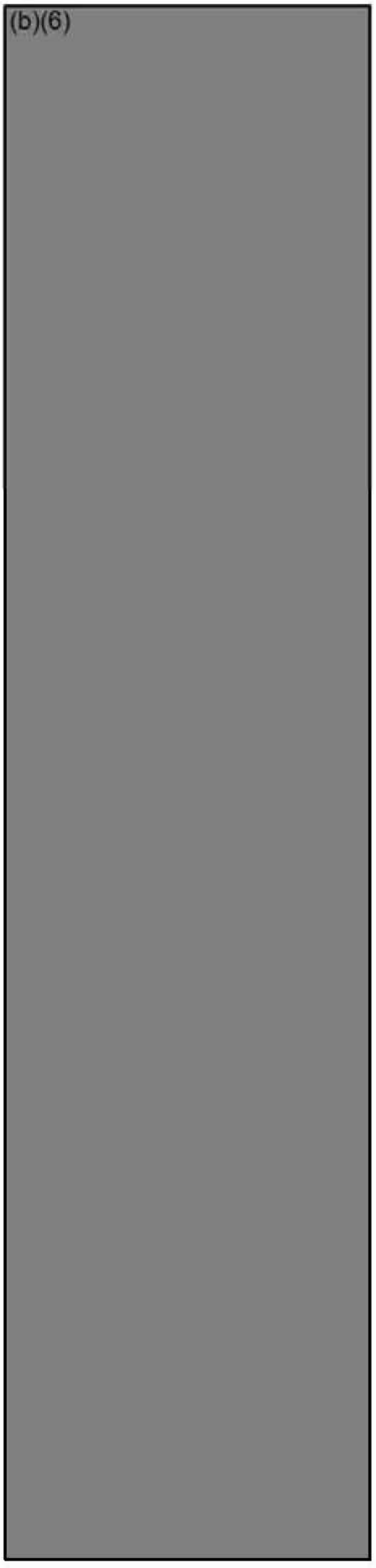
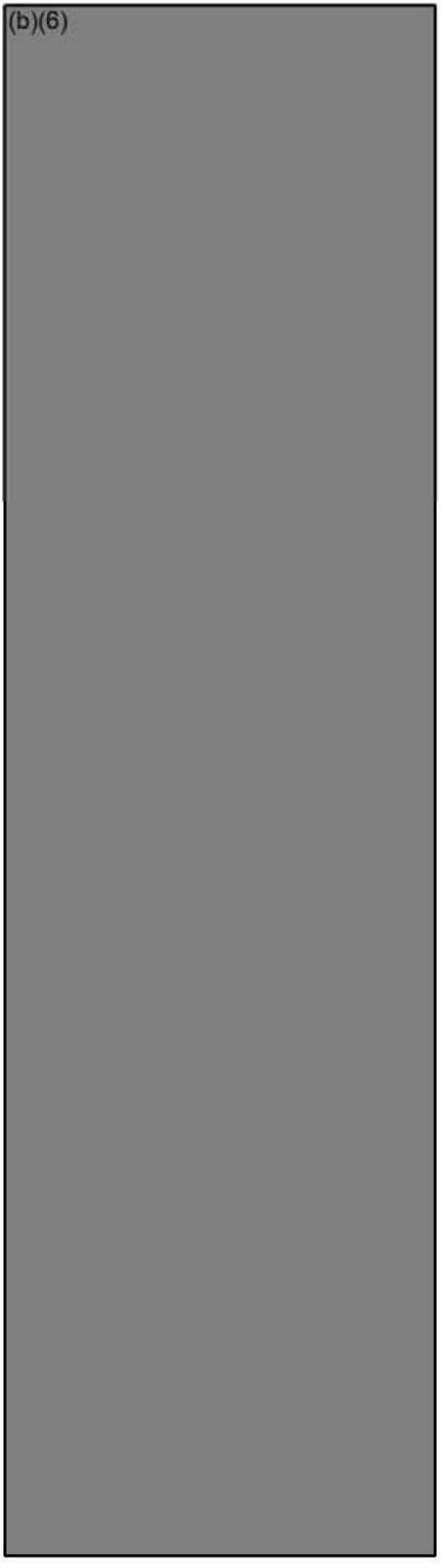
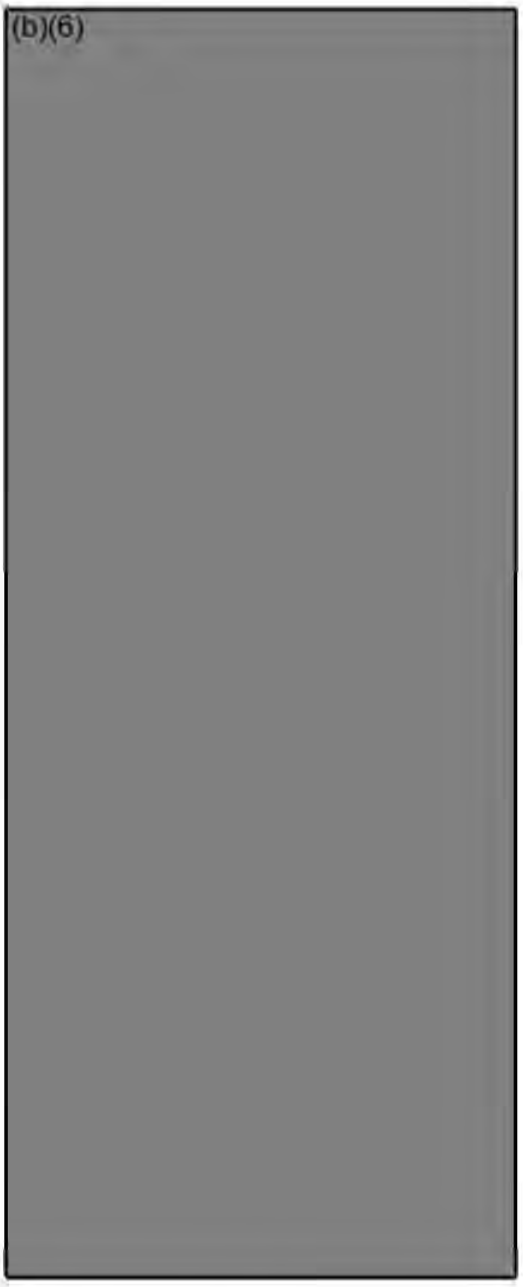

(b)(6)


(b)(6)



(b)(6) (b)(6)
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Department of
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(b)(6)
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(b)(

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(b)(6) MD, MPH

LCDR U.S. Public Health Service

Medical Officer

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National Center for Emerging and Zoonotic Infectious

Diseases Centers

for Disease Control
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Office Phone:
(b)(6)

BlackBerry:
(b)(6)

-----Original
Message-----

From: (b)(6)
(b)(6)
(b)(6)
(b)(6)

Sent: Tuesday,
August 18, 2015
4:16 PM

To: (b)(6)
(b)(6)

Cc: (b)(6) (b)(6)
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Hi [redacted] here is the version I sent you on 8/6. The journal (Drug Testing & Analysis) requested that we resubmit the manuscript by early September. Please let me know if you have any questions.

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[redacted]

[redacted] MD, MPH

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(b)(6)

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Was
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Did the
DoD
not
share

that
data or
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separat
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Regard
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even if
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are
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cript!

Where
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these
days?
Have
you
already
moved
?

Thanks
!

(b)(6)

MD, MPH

LCDR U.S. Public Health Service

Medical Officer

Enteric Diseases Epidemiology Branch

National Center for Emerging and Zoonotic Infectious Diseases

Centers for Disease Control and Preven

tion

Office Phone: (b)(6)

BlackBerry: (b)(6)

<Outbreak of Dietary Supplement-Associated Acute Hepatitis_Aug 5_Clean.docx>

Begin forwarded message:

From: (b)(6)
Subject: RE: OEP update
Date: December 3, 2015 at 12:55:18 AM EST
To: (b)(6)
(b)(6)

Cc: (b)(6)
(b)(6)

AFHSB can clear it in my absence through health affairs.

Best,

(b)

From: (b)(6)
Sent: Monday, November 30, 2015 7:31 PM
To: (b)(6)
(b)(6)
Cc: (b)(6)
(b)(6)
Subject: RE: OEP update

Thank you for re-sending your changes and for all of your input on the manuscript. We have actually already addressed your comments/edits and are currently updating the references to include the additional ones you provided.

Since the manuscript now includes information on the DOD cases, we wanted to know if additional DOD authors should be included beyond CDR (b)(6)

Also, what if any process still needs to be undertaken to have the document "cleared" by DOD?

As CDR (b)(6) mentioned, we have a very, very short window to be able to submit the manuscript to a supplemental issue of Drug Testing and Analysis focusing entirely on dietary supplements, so any information you could provide would be appreciated.

Best regards,

(b)(6) DVM, MPH
CDR, US Public Health Service
Health Studies Branch
National Center for Environmental Health
Centers for Disease Control and Prevention
4770 Buford Highway, MS F-57
Atlanta, GA 30341-3717
(o) (b)(6)
(bb) (b)(6)

(f) (b)(6)
(b)(6)

From: (b)(6) (b)(6) (b)(6)
Sent: Monday, November 30, 2015 12:26 PM
To: (b)(6)
Cc: (b)(6)
(b)(6)
Subject: Re: OEP update

I was the last one to edit I believe. I have sent it a number of times to Drs. (b)(6)
(b)(6) and (b)(6)

I am attaching again.

(b)(6)

(b)(6) (b)(6) PhD, MPH, FACSM
Professor and Director
Consortium for Health and Military Performance
A DoD Center of Excellence
Department of Military and Emergency Medicine
Uniformed Services University
4301 Jones Bridge Road
Bethesda, MD 20814
Office (b)(6)
FAX (b)(6)

On Nov 30, 2015, at 9:20 AM (b)(6) wrote:

Dear all,

Where do we stand? Who has this now? Is it in my court? I'm sorry to drop in without reading back over emails but I'm currently in the field.

Best,

(b)(6)

From: (b)(6)
Sent: Tuesday, November 24, 2015 4:59 PM
To: (b)(6)
(b)(6)
Cc: (b)(6)
Subject: FW: OEP update

Dear all,

Apologies for dropping out of this process. I've had a ton of travel and trouble-shooting since arriving here and am just getting comfortable with what my team is doing as we head into field tests for the upcoming national level survey roll- out.

(b)(6) was in touch with me last week to confirm our numbers from the active duty cases for the manuscript and they want to try to get it into the supplement issue. What do we need to do to clear this manuscript with DoD and how should we best proceed?

We also need to finalize our author list for CDC.

Best,

(b)(6)

(b)(6) DVM, PhD
Team Lead, Epi and Strategic Info Branch
Centers for Disease Control and Prevention – Zambia
Phone: (b)(6)
Mobile

From: (b)(6)
Sent: Tuesday, November 24, 2015 4:55 PM
To: (b)(6)
Cc:
Subject: OEP update

Hi (b)(6)

Thanks again for going over the OEP numbers with me on Friday. I talked with (b)(6) and we were correct—given our determination that DOD006 is a case and that DOD should NOT be counted as an OEP user, we will be updating the OEP manuscript shortly with a grand total of 92 cases, 69 of whom used OFP, 45 who were hospitalized, and 3 that were transplanted.

Since we are using DOD data now in the paper, do we need to plan to add any additional co-authors from DOD? And do you know what still needs to be done to clear the manuscript as far as DOD is concerned? To get it into the Drug Testing & Analysis

supplement we have to have it submitted by Dec. 7 so we are trying to figure out how much time DOD needs on their end.

Thanks for any help you can provide!!!

(b)(6)
DVM, MPH
CDR, US Public Health Service
Health Studies Branch
National Center for Environmental Health
Centers for Disease Control and Prevention
4770 Buford Highway, MS F-60
Chamblee, GA 30341
(o) (b)(6)
(bb) (b)(6)
(f) (b)(6)
(b)(6)

Begin forwarded message:

From: (b)(6)
Subject: RE: OEP update
Date: November 30, 2015 at 9:20:05 AM EST
To: (b)(6)
(b)(6)
Cc: (b)(6)
(b)(6)

Dear all,

Where do we stand? Who has this now? Is it in my court? I'm sorry to drop in without reading back over emails but I'm currently in the field.

Best,

(b)(

From: (b)(6)
Sent: Tuesday, November 24, 2015 4:59 PM
To: (b)(6)
(b)(6)
Cc: (b)(6)

Subject: FW: OEP update

Dear all,

Apologies for dropping out of this process. I've had a ton of travel and trouble-shooting since arriving here and am just getting comfortable with what my team is doing as we head into field tests for the upcoming national level survey roll- out.

(b)(6) was in touch with me last week to confirm our numbers from the active duty cases for the manuscript and they want to try to get it into the supplement issue. What do we need to do to clear this manuscript with DoD and how should we best proceed?

We also need to finalize our author list for CDC.

Best,

(b)(6)

(b)(6) E. (b)(6) DVM, PhD
Team Lead, Epi and Strategic Info Branch
Centers for Disease Control and Prevention – Zambia
Phone: (b)(6)
Mobile

From: (b)(6)
Sent: Tuesday, November 24, 2015 4:55 PM
To: (b)(6)
Cc:
Subject: OEP update

Hi (b)(6)

Thanks again for going over the OEP numbers with me on Friday. I talked with (b)(6) and we were correct—given our determination that DOD006 is a case and that DOD should NOT be counted as an OEP user, we will be updating the OEP manuscript shortly with a grand total of 92 cases, 69 of whom used OEP, 45 who were hospitalized, and 3 that were transplanted.

Since we are using DOD data now in the paper, do we need to plan to add any additional co-authors from DOD? And do you know what still needs to be done to clear the manuscript as far as DOD is concerned? To get it into the Drug Testing & Analysis supplement we have to have it submitted by Dec. 7 so we are trying to figure out how much time DOD needs on their end.

Thanks for any help you can provide!!!

(b)(6)
DVM, MPH
CDR, US Public Health Service
Health Studies Branch
National Center for Environmental Health
Centers for Disease Control and Prevention
4770 Buford Highway, MS F-60
Chamblee, GA 30341
(o) (b)(6)
(bb) (b)(6)
(f) (b)(6)
(b)(6)

Begin forwarded message:

From: (b)(6)
Subject: RE: Manuscript question
Date: August 18, 2015 at 3:42:48 PM EDT
To: (b)(6)
(b)(6)
Cc: (b)(6) (b)(6) (b)(6)

Can you resend the manuscript to me and cc (b)(6) (b)(6)

I want her input asap as well.

-----Original Message-----
From: (b)(6)
Sent: Friday, July 10, 2015 10:09 AM
To: (b)(6)
Cc:
Subject: RE: Manuscript question

Hi (b)(6) we definitely don't want to hijack your data if you're already working on a manuscript! But if you all don't foresee publishing the data, then it seems like it would be beneficial to include the DoD data in the national case-finding manuscript. I think the dietary supplement field is one field where any additional data will hopefully increase awareness, provide additional context to the issue, etc.

Let me know what you think. Thanks!
(b)(6)

(b)(6) (b)(6) MD, MPH
LCDR U.S. Public Health Service
Medical Officer

Enteric Diseases Epidemiology Branch
National Center for Emerging and Zoonotic Infectious Diseases Centers for Disease Control and Prevention Office Phone: (b)(6)
BlackBerry: (b)(6)

-----Original Message-----
From: (b)(6)
Sent: Friday, July 10, 2015 8:17 AM
To: (b)(6)
Cc:
Subject: Re: Manuscript question

happy to either finish the damn paper or include the data in your paper… i am in the midst of trainings and fiscal year hell but otherwise home still we don't move for awhile yet.

What do you think makes the most sense?

best,

(b)(

On Thu, Jul 9, 2015 at 4:55 PM, (b)(6) (b)((b)(6) wrote:

> Hi (b)(I received the dietary supplement manuscript back as a revise
> and resubmit. I think the biggest issue (noted by 1 reviewer and the editor) was the absence of the DoD case-patients. Here are some of the comments:
>
> 1. The rationale for excluding active duty military personnel seems
> weak.
>
> 2. The rationale for excluding active duty personnel does not seem to
> make sense. Other people included in the analysis might have very wide-ranging activity levels as well. Was this a logistical issue? Did the DoD not share that data or wish to publish separately? Regardless
>
> the specific reason, even if it's logistical, should be described. In addition, if the authors are aware of where this data is or where it will be published that should be included in the Discussion.
>
> Do you know if DoD is pursuing a manuscript? If not, then how do

you
think they'd feel about us including the data from the DoD case-patients? It would be relatively easy to rerun the same analysis and present the data in aggregate. Thoughts?

Sorry to keep pestering you about this manuscript!

Where are you these days? Have you already moved?

Thanks!

(b)(6)

(b)((b)(6) MD, MPH

LCDR U.S. Public Health Service

Medical Officer

Enteric Diseases Epidemiology Branch

National Center for Emerging and Zoonotic Infectious Diseases

Centers for Disease Control and Prevention

Office Phone: (b)(6)

BlackBerry: (b)(6)

6

Begin forwarded message:

From (b)(6)
(b)(6)
Subject: updated contact list (UNCLASSIFIED)
Date: October 29, 2013 at 12:24:13 PM EDT
To: (b)(6)
(b)(6)

Classification: UNCLASSIFIED
Caveats: NONE

Please find attached an updated contact list for the investigation. Please share as you deem appropriate.

Best,

(b)(

(b)(6) DVM, PhD, DACVPM
LCDR USPHS
Division of Integrated Biosurveillance (DIB)
Armed Forces Health Surveillance Center (AFHSC)
(b)(6) Tel (b)(6) Mobile
Fax

Classification: UNCLASSIFIED
Caveats: NONE

(b)(6)

7

Begin forwarded message:

From: (b)(6)
(b)(6)
Subject: supplement list (UNCLASSIFIED)
Date: December 16, 2013 at 3:26:02 PM EST
To (b)(6)

Classification: UNCLASSIFIED
Caveats: NONE

Here are the supplements listed on the questionnaires I have received

Best,

(b)(6)
DVM, PhD, DACVPM
LCDR USPHS
Team Lead, Epidemiology Response Team
Division of Integrated Biosurveillance (DIB)
Armed Forces Health Surveillance Center (AFHSC)
(b)(6) Tel| (b)(6) Mobile |
Fax

Classification: UNCLASSIFIED
Caveats: NONE

(b)(6)

8

Good morning Dr, (b)(6) thank you for your speedy response! Since this appears to be a joint effort between you and people from outside USU, can you clarify whose publication and presentation it was, please? From scrolling through a few of the emails and attachments, it appears that it may belong to the CDC, is this correct?

If it's not a a USU sponsored project, we may not legally be able to release the information, and we'd have to tell the requester who owns it so that they can request it from them directly. If it's not USU's can you please give me contact information (Organization name - if not CDC, and a name, title, email address, phone number, etc.)?

Thanks again

(b)(6)
CIV, USUHS
Program Administrative Specialist
Office of the VP for External Affairs, USUHS
(b)(6) - office
(b)(6) - fax

On Wed, Dec 7, 2016 at 9:41 PM (b)(6) wrote:

(b)(6)

I have forwarded all emails I have — (b) is in Kenya I believe and we are not in communication now. The abstract was minor — the publication I sent is far more thorough.

May of our interactions were in person or by phone
V/R
(b)

Begin forwarded message:

From: (b)(6)
Subject: OEP Hepatitis Cases Update
Date: November 15, 2013 at 4:05:10 PM EST
To: (b)(6)
(b)(6)

ALCON,

Across the Services, there have been 22 cases that meet case-ascertainment status for the CDC as probable or suspect cases. Of these, 21 have been interviewed. An additional 21 remain under investigation for case status. These have been identified through both reporting and active case-finding in DMSS for Active-Duty potential cases.

(b)(6)

Additionally, the Services have been distributed lists of non-Active-Duty beneficiaries for investigation as potential cases; a total of 117 potential cases were identified for further screening.

Attached is additional information:

1. Beneficiary active case finding slide showing the acute hepatitis cases found and their respective Service association.

2. Contact List of personnel involved in the OEP hepatitis case investigation, their phone numbers and email addresses.

3. FDA Oxyelite Product Guidance: information on what to send and where to send product samples to the FDA.

4. Ireland EIS update: An EIS update regarding the first case in Ireland.

By Service:

USCG

No Reported Cases

13 possible cases from the Active Duty case-finding in DMSS, of those 1 was a probable case and has been interviewed.

USN

Reported Cases: 6 (2 suspect and 4 probable) of those, 3 have been interviewed and 3 remain Persons Under Investigation (PUI).

NMCPHC received 95 AD Navy and Marine Corps ADSMs for follow-up from case-finding in DMSS, all were screened, 51 were excluded for not meeting case definition and 44 were investigated. 32 were not cases. From the 12 potential cases, 8 have been interviewed and 4 remain PUI

- 40 beneficiary cases have been identified for follow-up; screening pending on all 40 cases.

US Army

USAPHC received 58 AD from AFHSC, 1 was added in from a review of TRANSCOM records, and 1 was reported through MEDWATCH to total 58, so they have 60 to investigate. All 60 have been screened and 37 were excluded, 23 were investigated based on medical record review. From the review of cases, 6 were determined to be probable or suspect cases; 5 of those have been interviewed. 14 remain PUI and 3 were determined not to be cases based on interview.

- 55 beneficiary cases have been identified for follow-up; screening pending on all 55 cases.

USAF

-48/53 AD persons under investigation have been screened.

-2 AD patients were identified outside of the Active Case Finding (the OH and AZ cases)

-51 AD patients identified for follow-up via the Active Case Finding

-4 patients have met case definition; all 4 have been interviewed.

-22 Beneficiary cases have been identified for follow-up; screening pending on all 22 cases.

(b)(6)

I hoped we would have the next EXSUM on this topic, but it's not yet ready. Hopefully it will come out next week. There should be no problem sharing any data on these cases with state Public Health Departments or the CDC.

(b)(6)
Col, USAF, BSC

DVM, MPH, DACVPM

Director, Global Health Surveillance, Public Health Division

Defense Health Agency, Office of the Assistant Secretary of Defense

Defense Health Headquarters (DHHQ)

7700 Arlington Blvd.

Falls Church, VA 22042

Office (b)(6) ☎ (b)(6) ☎

**NEW EMAIL ADDRESS: NIPR: (b)(6) **

Begin forwarded message:

From (b)(6)
Subject: updated contact list (UNCLASSIFIED)
Date: October 29, 2013 at 12:24:13 PM EDT
To: (b)(6)
(b)(6)

Classification: UNCLASSIFIED
Caveats: NONE

Please find attached an updated contact list for the investigation. Please share as you deem appropriate.

Best,

(b)(6)

(b)(6) DVM, PhD, DACVPM
LCDR USPHS
Division of Integrated Biosurveillance (DIB)
Armed Forces Health Surveillance Center (AFHSC)
(b)(6) Tel (b)(6) Mobile
Fax

(b)(6)

Classification: UNCLASSIFIED
Caveats: NONE

Begin forwarded message:

From (b)(6)
Subject: supplement list (UNCLASSIFIED)
Date: December 16, 2013 at 3:26:02 PM EST
To: (b)(6)

Classification: UNCLASSIFIED
Caveats: NONE

Here are the supplements listed on the questionnaires I have received

Best,

(b)(6)
DVM, PhD, DACVPM
LCDR USPHS
Team Lead, Epidemiology Response Team
Division of Integrated Biosurveillance (DIB)
Armed Forces Health Surveillance Center (AFHSC)
(b)(6) Tel (b)(6) Mobile
Fax

Classification: UNCLASSIFIED
Caveats: NONE

Begin forwarded message:

From: (b)(6)
Subject: RE: Hepatitis and Liver Failure as a result to exposure to OxyELITE Pro supplement (UNCLASSIFIED)
Date: November 15, 2013 at 4:29:50 PM EST
To: (b)(6)
(b)(6)
Cc: (b)(6)
(b)(6)

Dr (b)(6) / Sgt (b)(6) - First, as LCDR (b)(6) mentioned, the Air Force investigation has only found 4 airmen with acute hepatitis who have an associated history of supplement usage. (Please debunk any myths that "51 Air Force members (nationally) took the supplement and became ill" as this is false and unfounded in our investigation.)

(b)(6) Air Force Preventive Medicine at AFMSA has released information for AF wide distribution. I've cc'd Co (AFMSA) here to see if an ANG Prov Med counterpart can contact you to discuss the information distribution within the ANG.

In the meanwhile, I've attached the email that went out through the line side from the AF/SG and most recent EXSUM (an updated one is expected soon). I also recommend the websites LCDR (b)(6) mentioned below.

Please let me know if you have any questions.
Thanks,

(b)(6)

LtCol (b)(6)

// SIGNED //
(b)(6) Lt Col, USAF, BSC
Chief, Epidemiology Consult Division
USAF School of Aerospace Medicine
Epidemiology Consult Service
USAFSAM/PHR
Wright-Patterson AFB, Ohio
Comm: (b)(6)
DSN (b)(6)
(b)(6)

-----Original Message-----
From: (b)(6)
(b)(6)
Sent: Friday, November 15, 2013 2:13 PM
To: (b)(6)
Cc: (b)(6)
(b)(6)
Subject: RE: Hepatitis and Liver Failure as a result to exposure to OxyELITE Pro supplement (UNCLASSIFIED)

Classification: UNCLASSIFIED
Caveats: NONE

Lt Col (b) is the main POC for the Air Force (USAFSAM). I am cc'ing her here.

There were 53 potential cases of acute hepatitis without other diagnosis that have been identified within the Air force, among these, only 4 have met case definition (which includes illness and supplement use).

In terms of learning more about supplement use within the Air Force or the broader DoD, a good resource is the http://hprc-online.org/ human performance resource center, housed within the Consortium for Health and Military Performance. Dr. (b)((b)(6) has been involved in the investigation and is a good resource. (b)(6) Some of their key resource on supplement safety are on this page http://hprc-online.org/about-us/about-hprc/dietary-supplements/opss. Also, there have been a few recent studies published on supplement use within the DoD.

Best,

(b)

(b)(6) DVM, PhD, DACVPM
LCDR USPHS
Division of Integrated Biosurveillance (DIB) Armed Forces Health Surveillance Center (AFHSC)
(b)(6) Tel (b)(6) Mobile
Fax

-----Original Message-----
From: (b)(6)
Sent: Friday, November 15, 2013 2:03 PM
To: (b)(6)
Cc:
Subject: RE: Hepatitis and Liver Failure as a result to exposure to OxyELITE Pro supplement

(b)(6)

Hello LCDR (b)(6) I'm the EIS officer assisting the Health Studies Branch in the supplement investigation. Dr (b)(6) who is an epi here at CDC and a reservist public health officer in the 165th Airlift Wing, contacted us with some DoD-specific questions regarding supplement use, education resources, etc. (see email below). I have cc'ed both Dr. (b)(6) and Sgt (b)(6) Would it be possible for you to identify the best individual to help answer their questions? I appreciate your help!

(b)(6) (b)(6) MD, MPH
LCDR US Public Health Service
EIS Officer
Health Studies Branch
Division of Environmental Hazards and Health Effects National Center for Environmental Health Centers for Disease Control and Prevention
Phone: (b)(6)

From: (b)(6)
Sent: Thursday, November 14, 2013 5:06 PM
To: (b)(6)
Cc:
Subject: Hepatitis and Liver Failure as a result to exposure to OxyELITE Pro supplement

Hi (b)(6) it was nice talking with you about the non-viral Hepatitis issue. As discussed, the GA National Guard bureau is concerned about use of the supplement and risk for non-viral Hepatitis among its active and reserve members. Apparently, there have been 51 Air Force members (nationally) who took the supplement and became ill. I spoke with Sgt (b)(6) today of the 165th Airlift Wing public health office in Savannah, GA. (I am a reservist public health officer with the wing). We/she have been tasked to find out how prevalent use of the supplement is in GA (among civilians) and more importantly, among fellow Air Force members. She has reached out to (b)(6) County health department and the GA State Health dept. (b)(6) sp?). The issues we could use your assistance are:

What types of educational material can be distributed by the GA Air National Guard about this issue?
Is there a prevalence estimate for usage of the supplement and resulting illness in GA?
Do you have (a) survey example(s) about usage of the supplement and resulting illness that Sgt (b)(6) could review and potentially administer to fellow Air Force members?
What resources are available on the internet?
Is there a D.O.D. or Air Force P.O.C. about this issue with who we could link Sgt (b)(6) ?
Are there any other efforts/contacts we should be made aware?

I have cc'd Sgt (b)(6)

Thank you for your assistance. (b)(6)

(b)(6) PhD, MPH
Epidemiologist
Lead Poisoning Prevention and Healthy Housing Division of Emergency and Environmental Health Services National Center for Environmental Health
Centers for Disease Control and Prevention
4770 Buford Highway, MS F-58
Atlanta, GA 30341
(b)(6) ph
(b)(6) fax
(b)(6) mailto (b)(6)

Classification: UNCLASSIFIED
Caveats: NONE

Forwarded message
From: (b)(6)
To: (b)(6)
(b)(6)

Date: Tue, 15 Oct 2013 09:04:30 -0500
Subject: FW: FDA warning message for widest distribution
Sir/Ma'am,
Please ensure the widest distribution. If any members are currently using OxyElite Pro they are urged to stop its use while an investigation of possible links between the product and acute hepatitis cases are evaluated.
V/R,
CMSg (b)(6)

*****Best Viewed in HTML*****

Wing/MDG CC's and MAJCOM/SG's,

Sent on behalf of the Air Force Surgeon General Public Affairs Office:

Airmen urged to heed FDA warning about dietary supplement

The U.S. Food and Drug Administration is advising consumers to stop using OxyElite Pro, a dietary supplement, because of suspected links to acute hepatitis.

The FDA, along with the Centers for Disease Control and Prevention and the Hawaii Department of Health are investigating reports of acute non-viral hepatitis in Hawaii where 29 cases are linked to a dietary supplement.

The FDA urges consumers to stop using the product while the investigation continues. Distributed by USPlabs LLC in Dallas, Texas, the product is sold nationwide in retail stores and on the internet.

"We are urging Airmen to stop using the product until the investigation concludes and results are confirmed," said Col. (b)(6) chief of Health Promotion, Air Force Medical Support Agency, Air Force Surgeon General.

There have been a total of 29 cases of acute non-viral hepatitis with an unknown cause reported in Hawaii. Eleven of the 29 patients have been hospitalized with acute hepatitis, two have received liver transplants and one person has died. The CDC is also investigating other cases of liver injury nation-wide that could be related.

(b)(6)

Symptoms of hepatitis include fever, fatigue, loss of appetite, nausea, vomiting, abdominal pain, dark urine, clay or gray-colored bowel movements joint pain, yellow eyes, and jaundice.

Per Col (b)(6)

Airmen who are experiencing these symptoms should contact their health care provider immediately. Many Airmen reportedly use dietary supplements for weight loss or muscle building. In 2011, one-third of Airmen reported using legal bodybuilding supplements in the past year, including 15 percent in the last month.

We encourage Airmen to get educated on dietary supplement safety through Operation Supplement Safety, the Department of Defense dietary supplement education and safety campaign.

Information about the campaign is found at: www.hprc-online.org/opss. Visit this link for more information about the FDA warning: http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm370857.htm .

The AF SG POC is Col (b)(6) (b)(6) (b)(6)

(b)(6) DAF

Director, Commander's Action Group

Air Force Medical Operations Agency

(b)(6) (COMM) (b) (DSN)

(b)(6)

3515 S. General McMullen

San Antonio, Tx 78266

Begin forwarded message:

From: (b)(6)
Subject: FWD: FW: EXSUM: Acute hepatitis cases associated with a dietary supplement (UNCLASSIFIED)
Date: October 15, 2013 at 8:00:37 AM EDT
To: (b)(6) (b)(6) (b)(6)

FYSA.

V/R
(b)(6)

----- Forwarded message -----
From: (b)(6)
Date: Fri, Oct 11, 2013 at 5:26 PM
Subject: FW: EXSUM: Acute hepatitis cases associated with a dietary supplement (UNCLASSIFIED)
To: (b)(6)

-----Original Message-----
From: USARMY NCR MEDCOM AFHSC Mailbox COMMCENTER
(b)(6)
Sent: Friday, October 11, 2013 1:09 PM
Subject: EXSUM: Acute hepatitis cases associated with a dietary supplement (UNCLASSIFIED)

Classification: UNCLASSIFIED
Caveats: NONE

Dear All,

Please find the attached EXSUM on acute hepatitis cases associated with a dietary supplement. This EXSUM has been provided for your situational awareness, and provides a summary of the current situation.

BLUF: Hawaii Department of Health reports 29 cases of acute non-viral hepatitis associated with use of a dietary supplement used for weight loss and for muscle gain. Two cases have been detected in active-duty Service members.

Best regards,

Division of Integrated Biosurveillance (DIB) Armed Forces Health Surveillance Center (AFHSC) U.S. Department of Defense
(b)(6)

(b)(6)

Classification: UNCLASSIFIED
Caveats: NONE

(b)(6)

(b)(6)
CDR, (b) USN
Commandant, SoM
Uniformed Services University
(b)(6)

Begin forwarded message:

From: (b)(6)
Subject: Contact list for the investigation into dietary supplement associated hepatitis (UNCLASSIFIED)
Date: October 25, 2013 at 3:45:25 PM EDT
To: (b)(6)
(b)(6)

Classification: UNCLASSIFIED
Caveats: NONE

All,

I have created a contact list for the relevant persons involved or who have been involved in this response. Please review for correctness, and send me pertinent additions or corrections if you have any changes.

Best,

(b)
(b)(6) DVM, PhD, DACVPM
LCDR USPHS
Division of Integrated Biosurveillance (DIB)
Armed Forces Health Surveillance Center (AFHSC)
(b)(6) Tel (b)(6) Mobile
Fax

Classification: UNCLASSIFIED
Caveats: NONE

Begin forwarded message:

From: (b)(6)
Subject: FW: supplement info for USAPHC newsletter (UNCLASSIFIED)
Date: December 3, 2013 at 11:00:51 AM EST
To: (b)(6)
(b)(6)

Classification: UNCLASSIFIED
Caveats: NONE

Hi (b)(6)

(b)(6) was so nice it was a pleasure to meet him last night. I am including text I am sending to USAPHC for their command newsletter if you have any comments.

Also- our last surveillance summary. Do you get these?

Best,

(b)(6)

-----Original Message-----
From: (b)(6)
Sent: Tuesday, December 03, 2013 10:59 AM
To: (b)(6)
(b)(6)
Cc: (b)(6)
Subject: supplement info for USAPHC newsletter (UNCLASSIFIED)

Classification: UNCLASSIFIED
Caveats: NONE

Thanks to (b)(6) for reviewing this already. I intend to provide this text to Ms (b)(6) for inclusion in their Commanders Newsletter.

I would appreciate thoughts or comments from DIB prior to sending this to her.

Best,

(b)(6)

(b)(6) DVM, PhD, DACVPM
LCDR USPHS
Team Lead, Epidemiology Response Team
Division of Integrated Biosurveillance (DIB)
Armed Forces Health Surveillance Center (AFHSC)
(b)(6) Tel (b)(6) Mobile
Fax

Classification: UNCLASSIFIED
Caveats: NONE

Classification: UNCLASSIFIED
Caveats: NONE

Begin forwarded message:

From: (b)(6)
Subject: Acute Hepatitis Case Status
Date: October 25, 2013 at 8:42:19 PM EDT
To: (b)(6)
(b)(6)

(b)(6)

(b)(6)

ALCON,

Below is information relative to the acute hepatitis cases associated with dietary supplements. Most of the information is plagiarized from others (and I thank them for it). Some information has been deleted for politically sensitivity reasons. Please feel free to correct anything contained within. Recommend the PH Centers at least make their Preventive Medicine specialists aware of the issue and of CDC's Health Advisory in an effort to communicate the problem to all Service Members and beneficiaries.

Attached is

1) AFHSC's 24 Oct EXSUM (which contains a good background of the situation).

2) CDC's 8 Oct Health Advisory Alert Network (HAN) Advisory

3) DoD's statement on the use of Dietary Supplements

4) A summary of what we know today (lengthy, but various offices supplied a lot of good information)

Current Status:

1) LCDR (b)(6) (AFHSC) is keeping a spreadsheet of events. She will amass a master list of cases, will have those identified through DMSS and the Services will provide those cases determined by other means.

2) Lt Col (b)(6) USAFSAM) is finalizing the questionnaire (based on CDC's, but with tweaks for the DoD) and the excel spreadsheet that the Services will use to follow up on

3) LCDR (b)(6) AFHSC) is sending Lt Col (b) some verbiage to satisfy concerns that service members will feel compelled to answer the questionnaire.

4) AFHSC Epi and Analysis will expand the DMSS search for other beneficiaries who fit the case definition. They will forward the list to NMCPHC for laboratory data, and send the list of additional potential cases to the Services for follow up.

5) The Services will be conducting their investigation into their Service-specific individuals who meet the screening case definition.

(b)(6)

6) AFHSC will be the collection point and analyzers for the Services' spreadsheets of questionnaire data.

(b)(6)

Note: Effective 1 Oct 2013, my email is: (b)(6)

(b)(6) Col, USAF, BSC

DVM, MPH, DACVPM

Director, Global Health Surveillance, Public Health Division

Defense Health Agency, Office of the Assistant Secretary of Defense

Defense Health Headquarters (DHHQ)

7700 Arlington Blvd.

Falls Church, VA 22042

Office (b)(6) ☎ (b)(6) ☎

NIPR: (b)(6)

SIPR: (b)(6)

Begin forwarded message:

From: (b)(6)
Subject: Most recent
Date: October 25, 2013 at 10:59:09 PM EDT
To: (b)(6)
Cc:

Not for distribution as is in "edit form"
(b)(6)

Begin forwarded message:

From: (b)(6)
Subject: Hepatitis investigation updated contact list (UNCLASSIFIED)
Date: November 13, 2013 at 3:50:33 PM EST
To: (b)(6)
(b)(6)

(b)(6)

(b)(6)

Classification: UNCLASSIFIED
Caveats: NONE

Here is the most updated contact list for the investigation

Best,

(b)(6)
DVM, PhD, DACVPM
LCDR USPHS
Division of Integrated Biosurveillance (DIB)
Armed Forces Health Surveillance Center (AFHSC)
(b)(6) Tel (b)(6) Mobile
Fax

Classification: UNCLASSIFIED
Caveats: NONE

Begin forwarded message:

From: (b)(6)
Subject: RE: Hepatitis Outbreak (UNCLASSIFIED)
Date: December 12, 2013 at 2:55:51 PM EST
To: (b)(6)
(b)(6)
Cc: (b)(6)

Classification: UNCLASSIFIED
Caveats: NONE

CAPT (b)(6)

Glad to have your expertise and I look forward to meeting you. I am attaching our surveillance summaries to describe the overall situation. If you would like more detail let me know and I will find something or we can discuss over the phone. I am still obtaining questionnaires and working to begin describing them for overall stats and basic univariate and bivariate analyses. If you have issues or thoughts on areas to focus or associations that should be investigated I would appreciate your insight!

I am also including the CDC questionnaire (we modified it to add in some DoD-specific categories such as rank and occupation). Case definitions were written up here: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6240a1.htm

Per the CDC we screened cases of acute unspecified hepatitis for supplement use, and lab values consistent with their case definition and ruled out chronic or other hepatic etiologies such as Wilson's or viral hepatitis. Alcoholism was captured in the questionnaire since we did much screening through record review vs through initial patient or physician contact (working through the Service public health centers). We also conducted active case-finding within Active Duty and beneficiary populations using the Defense Medical Surveillance System (DMSS) to look for ICD-9 codes consistent with acute unspecified hepatitis and ruling out ones with existing diagnoses for viral or other etiologies, these were checked for lab results around that acute hep diagnosis by the NMCPHC using their abilities to search HL7 lab data. Potential cases identified this way were classified as "positive" or "missing" if they didn't have lab data to rule them in or out, or "not positive" if they did not meet lab criteria. The Services followed up with record checks of the positive or missing categories and if they could not rule

them out for other diagnoses that might show up in places such as free text fields, then they were contacted and the checklist administered to make the final call on "suspect", "probable", or "not a case" per CDC direction. All those who met "Suspect" or "Probable" case classification were administered questionnaires (if they agreed to it).

I hope this makes sense!

Best,

(b)

-----Original Message-----
From: (b)(6)
Sent: Thursday, December 12, 2013 2:41 PM
To: (b)(6)
Cc: (b)(6)
Subject: Hepatitis Outbreak

Rob,

I am connecting you with LCDR (b) (b)(6) (PHS) who is running the DoD side of the investigation – she will respond with information you will need for background

Looking forward to meeting you and having you join us for 15 Jan meeting at 1400

Cheers
(b)

(b)(6) PhD, MPH, FACSM
Professor and Director
Consortium for Health and Military Performance
A DoD Center of Excellence
Department of Military and Emergency Medicine
USUHS
4301 Jones Bridge Road
Bethesda, MD 20814
Office (b)(6)
FAX (b)(6)

Classification: UNCLASSIFIED
Caveats: NONE

(b)(6)

DEPARTMENT OF DEFENSE (AFHSC)

Dietary Supplement-Associated Acute Hepatitis Surveillance Summary #1

18 NOV 2013, 1600 HRS EST (Next Report 25 NOV 2013)

9

Executive Summary

- **CASE REPORT:** As of 18 NOV 2013, 13 cases of acute hepatitis associated with use of weight-loss or muscle gain supplements have been identified in Active Duty (AD) Service members. AD cases have been reported from the US Army, Navy, Marine Corps, Air Force, and from the Coast Guard. An additional 10 potential AD cases remain under investigation. Nationally, there have been at least 29 cases reported from Hawaii. Additionally, the Centers for Disease Control and Prevention (CDC) has received 54 reports of possible supplement-associated acute hepatitis from 14 states other than Hawaii; 19 of these have been identified as cases. A case from Ireland was also reported to the World Health Organization (WHO).
- **ACTIONS:** AFHSC is coordinating closely with the Service public health centers, the CDC, and the Food and Drug Administration (FDA). Within the DoD, AFHSC, in conjunction with the Service public health centers, is conducting active case-finding for potential cases of supplement-associated acute hepatitis.
- **EXPOSURE:** OxyELITE Pro (OEP) has been removed from commissaries and from GNC stores on bases worldwide as of 17 OCT 2013. As of 10 NOV 2013, USPlabs LLC, of Dallas, Texas, recalled certain OEP dietary supplement products that the company markets, including those linked to acute hepatitis.
- **SAMPLING/CASE DEFINITION:** The case definition for cases of acute unspecified hepatitis associated with use of a weight-loss or muscle-gain dietary supplement is available in the 11 OCT 2013 CDC MMWR Notes from the Field. The FDA is collecting samples sent from persons who have used OEP, including unopened bottles, empty bottles, or opened and used product. Contact your Service public health center for more information on how to submit samples.

Background

- On 9 SEP 2013, the Hawaii Department of Health was notified of seven patients with severe acute hepatitis and fulminant liver failure of unknown etiology. Patients were previously healthy and sought medical care from MAY to SEP 2013. The seven patients had all used OxyELITE Pro, a dietary supplement sold nationwide that is marketed for weight loss and muscle gain, before illness onset.
- As of 17 NOV 2013, there are at least 29 cases reported from Hawaii. Fourteen other states have reported 54 possible supplement-associated hepatitis cases with an onset date between 10 APR and 15 OCT 2013 to the CDC. Of the 54 reports from states other than Hawaii, 19 have been confirmed as cases, 9 more remain under investigation, and the remaining 26 have been excluded as cases. Of the 19 confirmed cases, 16 took OEP.
- Within the DoD, a total of 23 potential cases among AD have been identified to date; 13 have been determined to be cases and 10 remain under investigation; seven of the 13 cases took OEP. Cases have been reported from the US Army, Navy, Marine Corps, Air Force, and the US Coast Guard.
- To date, there have been no deaths among identified cases. No cases have required a transplant; however, one case currently remains on a transplant list.
- Nationwide, case ascertainment has occurred through direct physician reporting, National Poison Center reporting, transplant list reviews, FDA MedWatch reports, and through active case-finding efforts.
- Within the DoD, reporting has occurred through medical event reporting. Additionally, the AFHSC has worked with the Services to perform active case-finding for AD cases since 14 NOV 2013.

Interagency / Global Actions

- AFHSC, the Defense Health Agency, USAFSAM, USAPHC, NMCPHC, the US Coast Guard, CDC, and FDA convene a weekly coordinating call at 1300 every Friday to discuss the outbreak and to coordinate the joint response. The next call will take place on 22 NOV at 1300.

DEPARTMENT OF DEFENSE (AFHSC)

Dietary Supplement-Associated Acute Hepatitis Surveillance Summary #2

29 NOV 2013, 1600 HRS EST (Next Report 5 DEC 2013)

10

Executive Summary

- **CASE REPORT:** As of 29 NOV 2013, 22 cases of acute hepatitis associated with use of weight-loss or muscle gain supplements have been identified in Active Duty (AD) Service members and 5 have been identified in beneficiaries. AD cases have been reported from the US Army, Navy, Marine Corps, Air Force, and from the Coast Guard. An additional 4 potential AD cases remain under investigation. Hawaii has identified 49 cases of supplement-related acute hepatitis. Additionally, the Centers for Disease Control and Prevention (CDC) has received 58 reports of possible supplement-associated acute hepatitis from 14 states other than Hawaii; 20 of these have been identified as cases. A case from Ireland was also reported to the World Health Organization (WHO). The majority of DoD cases are not included in the Hawaii or CDC case-counts.
- **ACTIONS:** AFHSC is coordinating closely with the Service public health centers, the CDC, and the Food and Drug Administration (FDA). Within the DoD, AFHSC, in conjunction with the Service public health centers, is conducting active case-finding for potential cases of supplement-associated acute hepatitis among Active Duty Service Members and other beneficiaries.
- **EXPOSURE:** OxyELITE Pro (OEP) has been removed from commissaries and from GNC stores on bases worldwide as of 17 OCT 2013. As of 10 NOV 2013, USPlabs LLC, of Dallas, Texas, recalled certain OEP dietary supplement products that the company markets, including those linked to acute hepatitis.
- **SAMPLING/CASE DEFINITION:** The case definition for cases of acute unspecified hepatitis associated with use of a weight-loss or muscle-gain dietary supplement is available in the 11 OCT 2013 CDC MMWR Notes from the Field. The FDA is collecting samples sent from persons who have used OEP, including unopened bottles, empty bottles, or opened and used product. Contact your Service public health center for more information on how to submit samples.

Background

- On 9 SEP 2013, the Hawaii Department of Health was notified of seven patients with severe acute hepatitis and fulminant liver failure of unknown etiology. Patients were previously healthy and sought medical care from MAY to SEP 2013. The seven patients had all used OxyELITE Pro, a dietary supplement sold nationwide that is marketed for weight loss and muscle gain, before illness onset.

National Case Summary:

- As of 29 NOV 2013, there are 49 cases reported from Hawaii; 41 (84%) used OEP. Fourteen other states have reported 58 possible supplement-associated hepatitis cases with an onset date between 10 APR and 15 OCT 2013 to the CDC. Of the 58 reports from states other than Hawaii, 20 have been confirmed as cases, 12 more remain under investigation, and the remaining 26 have been excluded as cases. Of the 20 confirmed cases, 17 (85%) took OEP.
- Nationwide, case ascertainment has occurred through direct physician reporting, National Poison Center reporting, transplant list reviews, FDA MedWatch reports, and through active case-finding efforts.

DoD Case Summary:

- As of 29 NOV 2013, a total of 301 potential cases of acute hepatic injury have been identified through reporting and through active case-finding by the AFHSC and by the Services. To date, 27 cases and potential cases have been reported to AFHSC; 202 have been excluded, 8 lost to follow-up or refused to participate, and 64 are pending investigation and case ascertainment.
- The majority of DoD cases are not included in the CDC or Hawaii case-counts.
- Within the DoD, a total of 22 cases among AD and five cases among beneficiaries have been reported; four potential cases remain under investigation. Cases and potential cases have been reported from the US Army (5 AD, 1 beneficiary), Navy (6 AD, 3 beneficiary), Marine Corps (6 AD), Air Force (4 AD, 1 beneficiary), and the US Coast Guard (1 AD).
- Questionnaires have been completed by 23 of the 27 AD and beneficiary cases; 16 (69.6%) out of 23 used OEP. The age range among cases with a completed questionnaire is from 20-45, with a mean age of 31; 61% were male.
- Among DoD cases, one AD case required a transplant; 15 have been hospitalized (13 AD, 2 beneficiary). To date, there have been no deaths among identified cases.
- Within the DoD, reporting has occurred through medical event reporting. Additionally, the AFHSC has worked with the Services to perform active case-finding for AD cases since 14 NOV 2013 and for non-AD beneficiaries since 21 NOV 2013.

Interagency / Global Actions

- AFHSC, the Defense Health Agency, USAFSAM, USAPHC, NMCPHC, the US Coast Guard, CDC, and FDA convene a bi-weekly coordinating call at 1300 every Friday to discuss the outbreak and to coordinate the joint response. The next call will take place on 6 DEC at 1300.

All information has been verified unless noted otherwise.
Sources include WHO, CDC, FDA, USAPHC, NMCPHC, USAFSAM, and the US Coast Guard.
For comments or additional information, please contact: (b)(6)

DEPARTMENT OF DEFENSE (AFHSC)

Dietary Supplement-Associated Acute Hepatitis Surveillance Summary #3

5 DEC 2013, 1600 HRS EST (Next Report 20 DEC 2013)

Executive Summary

- **CASE REPORT:** As of 5 DEC 2013, 26 cases of acute hepatitis associated with use of weight-loss or muscle gain supplements have been identified in Active Duty (AD) Service members and five have been identified in beneficiaries. AD cases have been reported from the US Army, Navy, Marine Corps, Air Force, and from the Coast Guard. Among civilian populations, there have been 49 cases reported from Hawaii (HI), and the Centers for Disease Control and Prevention (CDC) has identified 20 cases of supplement-associated acute hepatitis from 14 states other than HI. Additionally, a case from Ireland was reported to the World Health Organization (WHO).
- **ACTIONS:** AFHSC is coordinating closely with the Service public health centers, the CDC, and the Food and Drug Administration (FDA). Within the DoD, AFHSC, in conjunction with the Service public health centers, is conducting active case-finding for potential cases of supplement-associated acute hepatitis among AD Service members and other beneficiaries.
- **EXPOSURE:** OxyELITE Pro (OEP) has been removed from commissaries and from GNC stores on bases worldwide as of 17 OCT 2013. As of 10 NOV 2013, USPlabs LLC, of Dallas, Texas, recalled certain OEP dietary supplement products that the company markets, including those linked to acute hepatitis.
- **SAMPLING/CASE DEFINITION:** The case definition for cases of acute unspecified hepatitis associated with use of a weight-loss or muscle-gain dietary supplement is available in the 11 OCT 2013 CDC MMWR Notes from the Field. The FDA is collecting samples sent from persons who have used OEP, including unopened bottles, empty bottles, or opened and used product. Contact your Service public health center for more information on how to submit samples.

Background

- On 9 SEP 2013, the HI Department of Health was notified of seven patients with severe acute hepatitis and fulminant liver failure of unknown etiology. Patients were previously healthy and sought medical care from MAY to SEP 2013. The seven patients had all used OxyELITE Pro, a dietary supplement sold nationwide that is marketed for weight loss and muscle gain, before illness onset.

National Case Summary:

- As of 5 DEC 2013, there are 49 cases reported from HI; 41 used OEP. Fourteen other states have reported 67 possible supplement-associated hepatitis cases with an onset date between 10 APR and 15 OCT 2013 to the CDC. Of the 67 reports from states other than HI, 20 have been confirmed as cases, 19 more remain under investigation, and the remaining 28 have been excluded as cases. Of the 20 confirmed cases, 17 took OEP.
- Nationwide, case ascertainment has occurred through direct physician reporting, National Poison Center reporting, transplant list reviews, FDA MedWatch reports, and through active case-finding efforts.

DoD Case Summary:

- As of 5 DEC 2013, a total of 301 potential cases of acute hepatic injury have been identified through reporting and active case-finding by the AFHSC and individual Services. To date, 31 cases have been reported to AFHSC, 209 have been excluded, 6 lost to follow-up or refused to participate, and 55 are pending investigation and case ascertainment.
- The majority of DoD cases are not included in the CDC or Hawaii case-counts.
- Within the DoD, a total of 26 cases among AD and five cases among beneficiaries have been reported. Cases and potential cases have been reported from the US Army (9 AD, 1 beneficiary), Navy (6 AD, 3 beneficiaries), Marine Corps (6 AD), Air Force (4 AD, 1 beneficiary), and the US Coast Guard (1 AD).
- Questionnaires have been completed by 27 of the 31 AD and beneficiary cases, 3 have refused, and 1 is pending completion. The age range among cases with a completed questionnaire is from 20–45 with a mean age of 30; 65% were male.
- Among DoD cases, one AD case required a transplant; 18 cases have been hospitalized (16 AD, 2 beneficiaries). To date, there have been no deaths among identified cases. Among supplement users, 16 out of 27 used OEP; 9 OEP users took additional supplements. Total supplement use ranged from one to eight products, with a mean of two products used per case.
- Within the DoD, reporting has occurred through medical event reporting. Additionally, the AFHSC has worked with the Services to perform active case-finding for AD cases since 14 NOV 2013 and for non-AD beneficiaries since 21 NOV 2013.

Interagency / Global Actions

- AFHSC, the Defense Health Agency, USAFSAM, USAPHC, NMCPHC, the US Coast Guard, CDC, and FDA convene a bi-weekly coordinating call at 1330 every Friday to discuss the outbreak and to coordinate the joint response. The next call will take place on 6 DEC 2013 at 1330.

*** Legend: Text updated from the previous report will be printed in red; items unchanged from the previous Summary will be printed in black.**

All information has been verified unless noted otherwise.
Sources include WHO, CDC, FDA, USAPHC, NMCPHC, USAFSAM, and the US Coast Guard.
For comments or additional information, please contact (b)(6)

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~~UNCLASSIFIED//FOUO~~

EXECUTIVE SUMMARY

11 OCTOBER 2013

(U) ACUTE HEPATITIS ASSOCIATED WITH USE OF A DIETARY SUPPLEMENT. (U//~~FOUO~~) (MCAF-ZA) The Food and Drug Administration (FDA), the Centers for Disease Control and Prevention (CDC), and the Hawaii (HI) Department of Health (DOH) are investigating reports of acute non-viral hepatitis in HI associated with the use of a dietary supplement. On 9 SEP 2013, the HI DOH was notified of seven patients with severe acute hepatitis and fulminant liver failure of unknown etiology. Patients were previously healthy and sought medical care from MAY-SEP 2013. The seven patients had all used OxyELITE Pro, a dietary supplement sold nationwide that is marketed for weight loss and muscle gain, before illness onset. HI DOH has identified 29 patients meeting the case definition, described in a CDC Health Alert Network message: http://emergency.cdc.gov/HAN/han00356.asp. The Armed Forces Health Surveillance Center, in conjunction with the Service Public Health Centers, the CDC, and the FDA is working to identify potential cases within the DoD. Two active duty Service members have been identified who meet the CDC case definition. Suspected cases should be reported through Service public health centers and to local/state health departments. Service members should be reminded that dietary supplements are not regulated by the FDA, and should be used with caution.

(b)(6)

APPROVED BY: CDR (b)(6)
Armed Forces Health Surveillance Center

13

~~UNCLASSIFIED//FOUO~~

EXECUTIVE SUMMARY

24 OCT 2013

(U) ACUTE HEPATITIS AND LIVER FAILURE ASSOCIATED WITH USE OF DIETARY SUPPLEMENTS. (~~U//FOUO~~) (MCAF-ZA) Several organizations within the Department of Defense (DoD), along with the Centers for Disease Control and Prevention (CDC), are conducting an investigation into cases of acute non-viral hepatitis in active duty military personnel associated with the use of dietary supplements; specifically, OxyELITE Pro (OEP). The Armed Forces Health Surveillance Center and the Navy and Marine Corps Public Health Center began an active case-finding investigation to detect potential cases using CDC's case definition (http://emergency.cdc.gov/HAN/han00356.asp). In addition, the DoD has worked closely with CDC to develop a questionnaire for case investigation to be used by the Services. Since 9 SEP 2013, there have been 49 cases throughout the United States detected by the CDC and by state and local health departments through adverse event reporting and active case-finding. To date, five cases have been reported among active duty Service members in the DoD, and are included in the total count of 49 cases. Among DoD cases, four (80%) used OEP. As of 17 OCT 2013, OEP has been removed from DoD installations. Suspected cases should be reported through Service public health centers and to local or state health departments.

LCDR (b)(6)
(b)(6)

APPROVED BY (b)(6)
Armed Forces Health Surveillance Center

14

~~UNCLASSIFIED//FOUO~~

EXECUTIVE SUMMARY

24 OCT 2013

(U) ACUTE HEPATITIS AND LIVER FAILURE ASSOCIATED WITH USE OF DIETARY SUPPLEMENTS. ~~(U//FOUO)~~ (MCAF-ZA) Several organizations within the Department of Defense (DoD), along with the Centers for Disease Control and Prevention (CDC), are conducting an investigation into cases of acute non-viral hepatitis in active duty military personnel associated with the use of dietary supplements; specifically, OxyELITE Pro (OEP). The Armed Forces Health Surveillance Center and the Navy and Marine Corps Public Health Center began an active case-finding investigation to detect potential cases using CDC's case definition (http://emergency.cdc.gov/HAN/han00356.asp). In addition, the DoD has worked closely with CDC to develop a questionnaire for case investigation to be used by the Services. Since 9 SEP 2013, there have been 49 cases throughout the United States detected by the CDC and by state and local health departments through adverse event reporting and active case-finding. To date, five cases have been reported among active duty Service members in the DoD, and are included in the total count of 49 cases. Among DoD cases, four (80%) used OEP. As of 17 OCT 2013, OEP has been removed from DoD installations. Suspected cases should be reported through Service public health centers and to local or state health departments.

LCDR (b)(6)
(b)(6)

APPROVED BY: (b)(6)
Armed Forces Health Surveillance Center

DoD-modified Acute Liver Disease Case Questionnaire (25Oct13) State/Case ID:_____

Front Sheet for Department of Health
(May be removed for redacted documents)

Patient Information:

Name: _____

SSN: _____

DOB: _____

Phone number: _____

Street address: _____

City/State: _____

Current Military Installation Name: _____
Have you changed duty station since 1 April 2013? Y N
If yes, what was your prior duty station/location(s)?_____
_____

Component (select one): AD_____ Guard_____ Reserves_____ Other (list) _____
Beneficiary_____ (If Beneficiary, include FMP_____)

Service (select one): AF ____ Army ____ Marine Corps____ Navy_____ Other (list)_____

Rank: _____

Interviewed by: _____

Interviewer installation name:_____

Interviewer contact #s (DSN/Commercial):_____

INTRODUCTION

(Ask to speak with the case, if possible. Otherwise, ask to speak with their spouse/parent. Have a calendar with you).

Hello. My name is _____ and I'm calling from (Installation name) public health or preventive medicine office. We are looking into several cases of liver disease and investigating why people are becoming ill. We were notified that you (your family member) have (has) recently been sick with liver disease, and we would like to talk to you about your (their) illness and possible exposures you (they) might have had.

I'm calling as part of a Centers for Disease Control and Prevention nation-wide investigation. Have you already completed an interview with your local health department about your recent illness I mentioned above?

Yes____ No _____ Don't know _____

If patient answers Yes: **Could you give me the name of the person and office that interviewed you?**

_____

_____

Since you've already completed this questionnaire, I will not ask you to do it again. If you have any questions, you can contact me at _____. Thank you very much for your time.
(End of interview and contact the local Health Department for a copy of the questionnaire.)

If patient answers No or Don't know:

Participating in the questionnaire is completely voluntary. Your information will be kept confidential within the scope of this public health Investigation. If you are active duty, there will be no adverse action taken by your command if you decline to participate.

Would you be willing to answer our questions? It should take approximately 20-30 minutes. Most questions may be answered with a Yes, No, Don't Know, or I prefer not to answer. You are free to skip any questions you don't want to answer.

☐ **Yes – consent obtained from patient**

OR

☐ **Yes – consent obtained from parent or guardian (proxy)**

OR

☐ **Yes – consent obtained from other proxy (e.g. wife on behalf of husband)**
Relationship of proxy to patient: _____

OR

☐ **No - Case refused**

Thanks for agreeing to help us out. I'm going to be asking you some questions about the two months before your (your family member's) illness, so you might find it helpful to look at a calendar. Think back to when you (they) first felt sick.

1. **When did your symptoms begin?**
   Date: _____ (mm/dd/yyyy) □ Don't know/don't remember (go to 1a)

   1a. If you don't remember a date, do you remember which month or which week?
   Month _____ Date of Sunday of the specified week _____ (mm/dd/yyyy)

Answer options for the following section are Yes, No, Don't Know, or Prefer Not to Answer.

2. **During your illness, did you have any of the following symptoms?**

Nausea?	Y	N	Don't know	Refused
Vomiting?	Y	N	Don't know	Refused
Diarrhea?	Y	N	Don't know	Refused
Abdominal pain?	Y	N	Don't know	Refused
Fever?	Y	N	Don't know	Refused
Sweating at night?	Y	N	Don't know	Refused
Body aches?	Y	N	Don't know	Refused
Fatigue?	Y	N	Don't know	Refused
Loss of appetite?	Y	N	Don't know	Refused
Light or clay-colored stool?	Y	N	Don't know	Refused
Dark urine?	Y	N	Don't know	Refused
Yellow skin or yellow eyes?	Y	N	Don't know	Refused
Shortness of breath?	Y	N	Don't know	Refused
Fast heart rate?	Y	N	Don't know	Refused
Heart palpitations (irregular heart rate)?	Y	N	Don't know	Refused
Chest pain?	Y	N	Don't know	Refused
Dizziness?	Y	N	Don't know	Refused
Confusion?	Y	N	Don't know	Refused

Did you have any other symptoms I haven't asked about?

Y N Don't know Refused

If yes, list: a. _____

b. _____

c. _____

3. **Were you hospitalized for your illness?** Y N Don't know Refused
   ***If yes,* please indicate which medical treatment facilities where you were hospitalized:**
   Military hospital only_____ Civilian hospital only_____ Both Military and Civilian hospitals_____

4. **Were you given a diagnosis by a healthcare provider for your illness?**
   Y N Don't know Refused
   If yes, **What was the diagnosis?** _____
   ***If yes,* please indicate which medical treatment facilities gave you a diagnosis for your illness:**
   Military hospital only_____ Civilian hospital only_____ Both Military and Civilian hospitals_____

5. **Were you ever sick enough during your illness that you were considered for a liver transplant?**
   Y N Don't know Refused
   If yes, complete question 6. Other, skip to question 7.

6. **Did you receive a liver transplant?**
   Y N Don't know Refused

7. **Did you seek follow up care with any medical providers outside of the hospital or emergency department?**
   Y N Don't know Refused

   ***If yes,* please indicate which medical treatment facilities where you saw a physician:**
   Military hospital only_____ Civilian hospital only_____ Both Military and Civilian hospitals_____

8. **Prior to your illness, were you previously diagnosed by a healthcare provider with a liver problem, such as autoimmune hepatitis, primary biliary cirrhosis, Wilson's disease, or hemochromatosis?**
   Y N Don't know Refused
   If yes,
   Do you know the name of the problem, or your diagnosis? _____ Don't know

9. **Have you ever been diagnosed by a healthcare provider with any of the following conditions?**

Diabetes	Y	N	DK	Refused
Thyroid disease, such as hypothyroidism (low thyroid) or hyperthyroidism (overactive thyroid)	Y	N	DK	Refused
Heart disease	Y	N	DK	Refused
Kidney disease (such as renal insufficiency, renal failure, hemodialysis)	Y	N	DK	Refused
Cancer	Y	N	DK	Refused
Hypertension	Y	N	DK	Refused
Celiac disease (also known as 'celiac sprue')	Y	N	DK	Refused
Rheumatoid arthritis	Y	N	DK	Refused
Lupus	Y	N	DK	Refused

Did you have any other chronic conditions not listed here?

Y N Don't know Refused

If yes, list: a. _____

b. _____

c. _____

Now I want to ask you some questions about different exposures you might have had before you became ill. The next questions will cover just the two months before your symptoms began, so from _____ until your illness began. It may be helpful for you to get any supplements, herbal medications, or other medicine bottles for the next portion of the questionnaire.

10. During the two months before your symptoms began, did you take any nutritional supplements? This includes things like vitamins, calcium pills, weight loss pills, energy or muscle building products, energy drinks or shots, herbal or homemade remedies, etc.

Y N Don't know Refused

If yes, go to #11, otherwise skip to #14

11. During the two months before your symptoms began, did you use the product "OxyELITE Pro"?

Y N Don't know Refused

If yes, please complete the following:

Which OxyELITE Pro product did you use? *(If they used more than one of the products, complete an additional table for each product (see Appendix 1.))*	□ OxyELITE Pro (Original Formula) □ OxyELITE Pro (New Formula) □ OxyELITE Pro (Advanced Formula, Ultra-Intense Thermo) □ OxyELITE Pro Super Thermo Powder □ OxyELITE Pro Purple Top (Super Thermo) □ Other OxyELITE Pro Product (i.e. Don't remember which OxyELITE Pro product)
What was the primary reason you took OxyELITE Pro?	□ Lose weight □ Increase muscle gain □ Improve athletic performance □ Increase energy □ Other_____
How many tablets, scoops, or beverages did you take each day?	___ tablets per day **or** ___scoops per day ___drinks per day
What date did you start taking it?	_____ (mm/dd/yyyy)
What date did you stop taking it?	_____ (mm/dd/yyyy) [ ] still taking it
When did you buy the container of OxyELITE Pro that you were taking when your symptoms began?	_____ (mm/dd/yyyy)

Where did you buy the container of OxyELITE Pro that you were taking when your symptoms began? (select one below) On base: ☐ Off base: ☐ Internet: ☐ Other (list): ☐ (EX: mailed to me at my deployed location by a friend)	Store Name/Website: Address: City, State:
Do you have a membership/shoppers card with that store? *If yes*: Can you provide the number for us?	Y N Don't know Refused Number _____
Do you still have any of the OxyELITE Pro that you were taking when your symptoms began?	Y N Don't know Refused
If they have OxyELITE Pro left, ask them to please not throw it out, and answer next two questions. If they do not have any OxyELITE left, skip the next two questions and go to the last question on health effects.	
What is the OxyELITE Pro lot number on the bottle?	
Would you be willing to give us the remaining OxyELITE Pro that you were taking when your symptoms began for testing? *If yes,* what is the best way to reach you for further instructions?	Y N Don't know Refused _____ _____
Are you aware of any health effects associated with taking OxyELITE Pro? *If yes,* Please describe those health effects	Y N Don't know Refused _____ _____

12. Are you aware of anyone else (friends, family, coworkers, etc.) that also used OxyELITE Pro?

Y *(go to #12a and b)* N *(go to # 13)* Don't know *(go to #13)* Refused *(go to #13)*

***12a.* If you know of someone who uses OxyELITE Pro, would you be willing to provide contact information for them if needed?**

Y N Don't know Refused

If no, please consider notifying individual for them to consider discussing with the local health department.

***12b.* If you know of someone who uses OxyELITE Pro, do you know if they are ill with symptoms mentioned above?**

Y N Don't know Refused

13. During the two months before your symptoms began, did you use any other nutritional supplements? Remember this includes things like vitamins, calcium pills, weight loss pills, energy or muscle building products, energy drinks or shots, herbal or homemade remedies, etc.

Y N Don't know Refused

If yes, please complete the following, otherwise skip to #14:

(Please complete one table for EACH supplement reported. Use additional tables if they used multiple supplements (see Appendix 1).)

Product Name	_____
What was the primary reason you took the supplement?	□ Lose weight □ Increase muscle gain □ Improve athletic performance □ Increase energy □ Other_____

How many tablets, scoops, or beverages did you take each day?	___ tablets per day **or** ___scoops per day **or** ___drinks per day
What date did you start taking it?	_____(mm/dd/yyyy)
What date did you stop taking it?	_____(mm/dd/yyyy) [ ] still taking it
When did you buy the container of supplement that you were taking when your symptoms began?	_____(mm/dd/yyyy)
Where did you buy the container of supplement that you were taking when your symptoms began? (select one below) On base: ☐ Off base: ☐ Internet: ☐ Other (list): ☐	Store Name/Website: Address: City, State:
Do you have a membership/shoppers card with that store? *If yes*: Can you provide the number for us?	Y N Don't know Refused
Do you still have any of the product that you were taking when your symptoms began?	Y N Don't know Refused
If they have product left, ask them to please not throw it out.	
What is the product lot number on the bottle?	
Would you be willing to give us the remaining product that you were taking when your symptoms began for testing? *If yes,* what is the best way to reach you with further instructions?	Y N Don't know Refused _____ _____
Are you aware of any health effects associated with taking this supplement? *If yes,* Please describe those health effects	Y N Don't know Refused _____ _____

14. Did you take any prescription or over-the-counter medications, including Tylenol (also known as acetaminophen), regularly during the two months before your symptoms began?

Y N Don't know Refused

If yes:

(Please complete one table for EACH medication reported. Use additional tables if they used multiple medications (see Appendix 1).)

Product Name	_____
What date did you start taking it?	_____ (mm/dd/yyyy)
What date did you stop taking it?	[ ] _____ (mm/dd/yyyy) [ ] still taking it
What was your dose? (eg. 2 pills or 500mg)	_____ or Unknown
How often did you take it?	Every day A few times per week A few times per month Never Other (*please specify)*_____

	Don't know Refused

The next several questions ask about behaviors that may affect the liver.

15. Did you eat any mushrooms that were gathered from the wild by you or someone you know during the two months before your symptoms began?

Y N Don't know Refused

16. Did you use tobacco during the two months before your symptoms began?

Y *(go to #16a.)* N Don't know Refused

16a. Approximately how many tobacco products did you use per day or per week?

Cigarettes: Number per day _____ **OR** Number per week _____
Smokeless tobacco: Number per day _____ **OR** Number per week _____
Other: Number per day _____ **OR** Number per week _____

17. Did you drink alcohol during the two months before your symptoms began?

Y N Don't know Refused

If yes,

How many days in the average week did you drink alcohol?

_____ days

How many servings of alcohol did you have at each sitting? (One serving is equal to one glass of wine, one can/bottle of beer, or one shot.)

_____ servings

18. *(Question Deleted by DoD)*

Now I would like to obtain some basic information about you.

19. What is your age? _____ years

20. What is your sex? M F

21. What is your height? _____feet_____inches

22. What is your weight? _____pounds

23. Which one or more of the following would you say is your race?

- ☐ **White** (*skip to question #28)*
- ☐ **Black or African American** (*skip to question #28)*
- ☐ **American Indian or Alaska Native** (*skip to question #28)*
- ☐ **Asian** *(go to question #24)*
- ☐ **Pacific Islander** *(go to question #24)*
- ☐ **Other** (*skip to question #28)*
- ☐ **Don't know/Refused** (*skip to question #28)*

If Asian or Pacific Islander, go to question #24. If other race, skip to #28.

24. With what groups or nationalities do you associate your cultural heritage (for example, Native Hawaiian, Japanese, Filipino?) _____

25. In what country were you born? _____

26. In what country or countries have you lived?

_____

_____

27. During the two months before your symptoms began, did you consume any foods, herbs, or other products that you used as part of traditional cultural practice? Y N Don't know Refused

If yes, Please describe:

_____

28. Are you of Hispanic, Latino, or Spanish origin: Y N Don't know Refused

29. Have you ever lived in Hawaii for at least 6 months? Y N Don't know Refused

***30.* What was your occupation during the two months before your symptoms began?** _____

31. Did you travel out of the state for work or pleasure since 1 April 2013?

Y N Don't know Refused

If yes,

Please indicate all locations you travelled/vacationed to:_____

_____

32. Were you deployed out of the country at anytime from January 2013 to present to PACOM, CENTCOM, SOUTHCOM, or AFRICOM?

Y N Don't know Refused

If yes, **please indicate the country/installation/approximate dates :**

_____

That is all of the questions we have for now; thank you very much for your time. This information will help us try to resolve the cause of your illness. As we learn more about this situation, we may have more information to share with you or additional questions to ask you. Would it be all right to contact you again if more information is needed?

Y N *If yes,* **What would be the best way to reach you?** _____

In the future, we recommend that you discuss the use of any nutritional supplements with your healthcare provider.

Your local health department may contact you to conduct this same interview. To prevent you from repeating this questionnaire, please let them know they can contact me at _____.

Please call our office at _____if you have any further questions and again, thank you for your help!

Appendix 1. Extra Supplement and Medication Tables

Additional Oxy-Elite Pro Supplement Form

(Please complete one table for EACH OxyELITE Pro product reported. Use additional tables if they used multiple products.)

Which OxyELITE Pro product did you use?	□ OxyELITE Pro (Original Formula) □ OxyELITE Pro (New Formula) □ OxyELITE Pro (Advanced Formula, Ultra-Intense Thermo) □ OxyELITE Pro Super Thermo Powder □ OxyELITE Pro Purple Top (Super Thermo) □ Other OxyELITE Pro Product (i.e. Don't remember which OxyELITE Pro product)
What was the primary reason you took OxyELITE Pro?	□ Lose weight □ Increase muscle gain □ Improve athletic performance □ Increase energy □ Other_____
How many tablets, scoops, or beverages did you take each day?	___ tablets per day **or** ___scoops per day ___drinks per day
What date did you start taking it?	_____ (mm/dd/yyyy)
What date did you stop taking it?	_____ (mm/dd/yyyy) [ ] still taking it
When did you buy the container of OxyELITE Pro that you were taking when your symptoms began?	_____ (mm/dd/yyyy)
Where did you buy the container of OxyELITE Pro that you were taking when your symptoms began? (select one below) On base: ☐ Off base: ☐ Internet: ☐ Other (list): ☐	Store Name/Website: Address: City, State:
Do you have a membership/shoppers card with that store? *If yes*: Can you provide the number for us?	Y N Don't know Refused Number _____
Do you still have any of the OxyELITE Pro that you were taking when your symptoms began?	Y N Don't know Refused
If they have OxyELITE Pro left, ask them to please not throw it out.	
What is the OxyELITE Pro lot number on the bottle?	
Would you be willing to give us the remaining OxyELITE Pro that you were taking when your symptoms began for testing? *If yes,* what is the best way to reach you for further instructions?	Y N Don't know Refused _____ _____
Are you aware of any health effects associated with taking OxyELITE Pro? *If yes,* Please describe those health effects	Y N Don't know Refused _____ _____

Additional Supplements Form

(Please complete one table for EACH supplement reported. Use additional tables if they used multiple supplements.)

Product Name	_____
What was the primary reason you took the supplement?	□ Lose weight □ Increase muscle gain □ Improve athletic performance □ Increase energy □ Other_____
How many tablets, scoops, or beverages did you take each day?	___ tablets per day **or** ___scoops per day **or** ___drinks per day
What date did you start taking it?	_____(mm/dd/yyyy)
What date did you stop taking it?	_____(mm/dd/yyyy) [ ] still taking it
When did you buy the container of supplement that you were taking when your symptoms began?	_____(mm/dd/yyyy)
Where did you buy the container of supplement that you were taking when your symptoms began? (select one below) On base: ☐ Off base: ☐ Internet: ☐ Other (list): ☐	Store Name/Website: Address: City, State:
Do you have a membership/shoppers card with that store? *If yes*: Can you provide the number for us?	Y N Don't know Refused
Do you still have any of the product that you were taking when your symptoms began?	Y N Don't know Refused
If they have product left, ask them to please not throw it out.	
What is the product lot number on the bottle?	
Would you be willing to give us the remaining product that you were taking when your symptoms began for testing? *If yes,* what is the best way to reach you with further instructions?	Y N Don't know Refused _____ _____
Are you aware of any health effects associated with taking this supplement? *If yes,* Please describe those health effects	Y N Don't know Refused _____ _____

Additional Prescription or OTC Medication Form

(Please complete one table for EACH medication reported. Use additional tables if they used multiple medications.)

Product Name	____
What date did you start taking it?	__________________________ (mm/dd/yyyy)
What date did you stop taking it?	[ ] ________________________ (mm/dd/yyyy) [ ] still taking it
What was your dose? (eg. 2 pills or 600mg)	_______________ or Unknown
How often did you take it?	Every day A few times per week A few times per month Never Other *(please specify)*______________________ Don't know Refused

Product Name	____
What date did you start taking it?	__________________________ (mm/dd/yyyy)
What date did you stop taking it?	[ ] ________________________ (mm/dd/yyyy) [ ] still taking it
What was your dose? (eg. 2 pills or 600mg)	_______________ or Unknown
How often did you take it?	Every day A few times per week A few times per month Never Other *(please specify)*______________________ Don't know Refused

Product Name	____
What date did you start taking it?	__________________________ (mm/dd/yyyy)
What date did you stop taking it?	[ ] ________________________ (mm/dd/yyyy) [ ] still taking it
What was your dose? (eg. 2 pills or 600mg)	_______________ or Unknown
How often did you take it?	Every day A few times per week A few times per month Never Other *(please specify)*______________________ Don't know Refused

Checklist for Potential Cases Identified Within the DoD

1. Did the patient present with acute onset hepatitis of **unknown etiology** that developed on or after April 1, 2013?

No (Stop, not a case) Yes (Go to question # 2)

~~2. Did the patient use a non-prescription weight loss or muscle building dietary or nutritional supplement during the 60 days prior to illness onset?~~

~~No (Stop, not a case) Yes (Go to question # 3)~~

~~3.~~ 2. Does the patient have an ALT ≥ 4 times the upper limit of normal AND a total bilirubin ≥ 2 times the upper limit of normal?

No (Stop, not a case) Yes (Go to question # 4)

~~4.~~ 3. Does the patient have a negative workup for infectious hepatitis and any other explicative/likely etiology?

No (stop, not a case yet, hospital should continue workup) Yes (Go to question # 5)

~~5.~~ 4. Does the patient have

a. Hepatic imaging (i.e., ultrasound/doppler, CT scan, or MRI) findings **INCONSISTENT** with another explicative/likely etiology?	No	Yes
b. A negative viral hepatitis panel?	No	Yes
~~c.~~ No pre-existing diagnosis of chronic liver disease (e.g. ~~autoimmune~~ ~~d.~~ c. ~~hepatitis,~~ primary biliary cirrhosis, primary sclerosing cholangitis, Wilson's disease, hemochromatosis)	No	Yes
~~e.~~ d. No history of recent hypotensive shock or septic episodes	No	Yes
~~f. No history of chronic alcoholism~~	~~No~~	~~Yes~~

If yes to all 5a, 5b, 5c, and 5d ~~and 5e~~ then this is a probable case. If anything else, this is a suspect case.

Case Definitions:

Probable Case

An individual with acute-onset hepatitis of unknown etiology that developed symptoms on or after April 1, 2013 following use of a non-prescription weight loss or muscle building dietary or nutritional supplement during the 60 days prior to illness onset.

With acute-onset hepatitis of unknown etiology defined as having BOTH:

- ALT ≥ 4 times the upper limit of normal
- Total bilirubin ≥ 2 times the upper limit of normal

AND negative workup for infectious and any other explicative etiologies for hepatitis with documentation of ALL of the following:

- Hepatic imaging (i.e. ultrasound/doppler, CT scan, MRI) not consistent with alternative, explicative etiologies
- Negative viral hepatitis panel
- No pre-existing diagnosis of chronic liver disease (e.g., autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, Wilson's disease, hemochromatosis)
- No recent hypotensive shock or septic episodes
- No history of alcoholism documented in medical records

Suspected Case

An individual that meets the criteria for a probable case, but does not have complete documentation of a negative workup for infectious or other etiologies as listed above.

17

Acute Hepatitis Linked to Dietary Supplement Use

KEY MESSAGE: Since 1 Apr 2013, a number of previously healthy individuals developed acute hepatitis and sudden liver failure of unknown cause after using a dietary supplement for weight loss or muscle building. The Centers for Disease Control (CDC) recommends increased vigilance by public health agencies, emergency departments, and healthcare providers for patients who develop acute hepatitis or liver failure following use of a weight loss or muscle building nutritional supplement. On 8 Oct 2013 the Food and Drug Administration (FDA) and CDC issued advisory messages warning against the use of certain dietary supplements following reports of cases of acute hepatitis in Hawaii. DoD is following the lead Federal Agencies, FDA and CDC, and joined the investigation and safety messaging actions. The Defense Health Agency, Armed Forces Health Surveillance Center, Military Service Public Health Centers, Human Performance Resource Center, and CDC will continue to work collaboratively on the cases, and will hold teleconferences as needed.

KEY POINTS:

- On 9 Sep 2013, the Hawaii Department of Health (HDOH) was notified of seven patients with severe acute hepatitis and fulminant liver failure of unknown etiology. Patients were previously healthy and sought medical care during May-September 2013. Clinicians reported that the seven patients had all used Oxy ELITE Pro™ (OEP), a dietary supplement marketed for weight loss and muscle gain, before illness onset.
- As of 23 Oct 2013, the CDC has received reports of 49 potential cases from several states, including cases from the DoD. Currently, the majority of confirmed cases are located in Hawaii.
- CDC has been asking about over-the-counter, traditional and prescription medications, home remedies, and herbal and dietary supplements in addition to OEP, and is looking at the data; so far no other product appears to be strongly associated as a potential cause or factor.
  - — Of cases reported to the HDOH and CDC in response to a public health alert, the majority had used OEP. Almost all cases identified on the mainland outside of Hawaii had OEP use history. There appears to be a racial preponderance, however the investigation is ongoing and it is unclear whether this trend will hold. Although CDC does not yet have information on the majority of mainland reports, among cases where race is known and who took OEP, almost all are Asian or Pacific Islander.
- The DoD used DMSS to find Active Duty (AD) cases meeting the CDC case definition and has identified 48 potential cases among DoD health care beneficiaries (based on HL7 lab and liver function data to include total bilirubin and ALT, and absence of other diagnoses (except newly diagnosed autoimmune hepatitis which may share some common laboratory and histological findings) for further investigation.
  - Active surveillance using medical data initially identified 281 potential cases with diagnoses of unexplained hepatitis since 1 Apr 2013. The list was further narrowed down by AFHSC and NMCPHC to 140 potential cases among the Active Duty population, of which 92 had incomplete laboratory data, for follow-up between the Services and AFHSC.

- AFHSC has begun to search for cases among DoD healthcare beneficiaries (in addition to Active Duty) evaluated or treated in MTFs using medical data.
- The DoD Services will focus on the 48 cases first, then expand to the remaining 140 cases over the next 2-4 weeks, with subsequent investigation of the dependent/beneficiary population. The Services have been sent the list of their potential cases for further investigation. DoD/AFHSC has worked closely with CDC to develop a questionnaire for case investigation to be used by the Services. CDC will share any data from DoD cases that they may come across in their investigation.

- DoD health care providers have reported six cases with acute hepatitis meeting the CDC case definition. Among the DoD cases, 5/6 used OEP, the sixth used a different supplement for weight loss and is being considered a case by the HI DOH
  - — AD Sailor (24yo male Japanese/Hawaiian) in Virginia (from Hawaii) discharged from MCV in Richmond and being treated as an outpatient for hepatitis. Need for a liver transplant now appears averted due to continued stabilization. He has plans to return to Hawaii based on the follow-up outcome. Reportedly purchased OEP at Pearl Ridge Mall GNC (not the Navy Exchange).
  - — AD Airman (37yo male Asian) treated for hepatitis (with autoimmune features) as an outpatient (discharged from Univ. of Cincinnati) and continues improving. Reportedly purchased OEP at Wright-Patterson AFB, and was interviewed by FDA investigators.
  - — AD Soldier (25yo female) evaluated for acute hepatitis as an outpatient by Tripler Army Medical Center (TAMC) in Sep 2013, associated with the use of the dietary supplement "True-Slim," a herb tea product marketed for weight loss which she took for about two months before her symptom onset. She has returned to duty, and her liver function tests have continued to improve.
  - — AD Chief Petty Officer (female) admitted to Naval Medical Center San Diego with severe hepatitis and coagulopathy likely from OEP/supplement-related drug-induced liver injury. She is being evaluated for potential need of liver transplant.
  - — AD Marine (22yo male) admitted to Naval Hospital Twenty-Nine Palms for acute hepatitis on 16-18 Oct 2013 who had been taking OEP approximately 4 weeks prior to illness onset.
  - — AD Sailor (29yo male) who presented to TAMC 5 Jun 2013 with diagnosis of drug induced hepatitis. He subsequently PCSed onboard the USS Reagan. Upon follow-up questioning, he stated he used OEP which he got from bodybuilder.com.

- CDC investigation shows a link to the consumption of OEP, marketed for weight loss and work-out enhancement, and issued a Health Advisory Network alert on 8 Oct 2013.
  - However, CDC investigators continue to collect data on possible cases that use any "non-prescription weight loss or muscle building dietary or nutritional supplement" during the 60 days prior to illness.
- On 11 Oct the FDA advised consumers not to use any dietary supplements labeled OEP or VERSA-1 because these products contain an ingredient, aegeline, for which the manufacturer has not provided adequate evidence of safety; DoD is issuing the same message. The initial FDA advisory, issued 8 Oct 2013, was for OEP only.
- FDA issued a warning letter to USP Labs, Inc. regarding the ingredient in two products, OEP and VERSA-1, on 11 Oct 2013. The FDA investigation has focused on the ingredient aegeline, also referred to as N-[2-hydroxy-2(4-methoxyphenyl) ethyl]-3-phenyl-2-propenamide.
  - The FDA warning letter asks USP Labs, Inc. to confirm that aegeline is a "dietary ingredient" under 21 U.S.C. 321(ff)(1) for which a notification is required under 21 U.S.C. 350b(a)(2) and 21 CFR 190.6, if present in the food supply as an article used for food in a form in which the food has not been chemically altered or there is a history of use or other evidence of safety provided to FDA prior to marketing. Otherwise, aegeline is an adulterant. The company has two weeks to respond to the FDA.
  - This warning letter is similar to the 2012 FDA warning letter issued to the same company regarding DMAA. USP Labs, Inc., recently reformulated OEP removing 1,3-dimethylamylamine (DMAA) from this supplement and others, following the April 2013 FDA determination that DMAA is not a legal dietary supplement ingredient.
  - To identify and track cases and potential cases, the FDA is using MEDWATCH, and CDC is using the National Poison Data System (NPDS) and CDC Hot Line.
  - DoD is using DMSS for passive surveillance and OPSS messaging for active surveillance of cases and potential cases.
- To identify and track cases and potential cases, the FDA is using MEDWATCH, and CDC is using the National Poison Data System (NPDS) and has issued a call for cases through several relevant professional groups.
- DoD is using DMSS for passive surveillance and OPSS messaging for active surveillance of cases and potential cases.
- By 17 Oct 2013, GNC stores removed four products (OEP, VERSA-1, Craze, and Detonate) from military installation stores.
  - OEP and VERSA-1 contain aegeline, according to the FDA Warning Letter to USP Labs, Inc. (Ref: Oct 11, 2013 Warning Letter online at http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2013/ucm371203.htm)

- Craze and Detonate contain another compound, identified by researchers and not mentioned in current FDA and CDC messaging. Researchers in the US and overseas found N,alpha-diethylphenylethylamine (N, α-DEPEA), a methamphetamine analog in samples of Craze and Detonate (Ref: Cohen et al., online at http://onlinelibrary.wiley.com/doi/10.1002/dta.1578/pdf and [definitive source article not yet procured].

- It is DoD policy to "provide appropriate dietary supplements to Service members where indicated" and to "provide education and training to Service members in order to ensure that they are able to make healthy lifestyle choices regarding nutrition and dietary supplements and so achieve and maintain performance and health" in accordance with DoD Instruction 6130.05, "DoD Nutrition Committee".

- The Military Service Secretaries are responsible for providing "military-specific education and training to Service members on the benefits of adequate and appropriate nutrition and the use of and potential harm from dietary supplements, taking into consideration relevant recommendations of the DoD Nutrition Committee", in accordance with DoD Instruction 6130.05, "DoD Nutrition Committee".

- The Dietary Supplements and Other Self-Care Products Subcommittee of the DoD Nutrition Committee "shall make policy recommendations to the Military Services and other DoD beneficiary groups regarding the use of dietary supplements, where indicated, in areas including, but not limited to: (1) Dietary supplement education; (2) Military-specific research; (3) Adverse event reporting and monitoring; (4) Human performance optimization; (5) Military Service special operations; (6) Identification of research gaps and requirements; and (7) Identification of opportunities for resource sharing and cost containment among the Military Services." IAW DoDI 6130.05.

RECENT CONGRESSIONAL INTEREST:

- Senator (b)(6) s office expressed interest in the content of draft DoD policy on dietary supplements after a developmental draft was shared with the Military Exchanges for review. DoD policy regarding dietary supplements is contained in DoD Instruction 6130.05, "DoD Nutrition Committee". Additional draft policy under consideration remains in development.

QUESTIONS and ANSWERS:

- **What happened to the cases in DoD?**

  All identified cases are being treated and seem to be recovering.

- **Who directed the removal of these dietary supplements from stores on military installations?**

  The manufacturer (USP Labs, Inc.) and vendor (GNC) removed two products, each of which contains the ingredient that is the focus of FDA's warning letter to USP Labs, Inc.

- **What is DoD doing to protect Service members and families from unsafe dietary supplements like these?**

  DoD and the Military Services implemented Operation Supplement Safety educational program during the summer of 2013. Dietary supplement safety educational outreach directed to both consumers and medical professionals is occurring in military treatment facilities, dietician offices, gyms, and online via the Human Performance Resource Center and Operation Live Well.

- **What is a dietary supplement?**

  A product (other than tobacco) that is intended to supplement a diet that bears or contains one or more of these dietary ingredients: a vitamin; a mineral; an herb or other botanical; an amino acid; a dietary substance for use by humans to supplement the diet by increasing the total daily intake of that substance; or a concentrate, metabolite, constituent, or extract, or combinations of these ingredients.

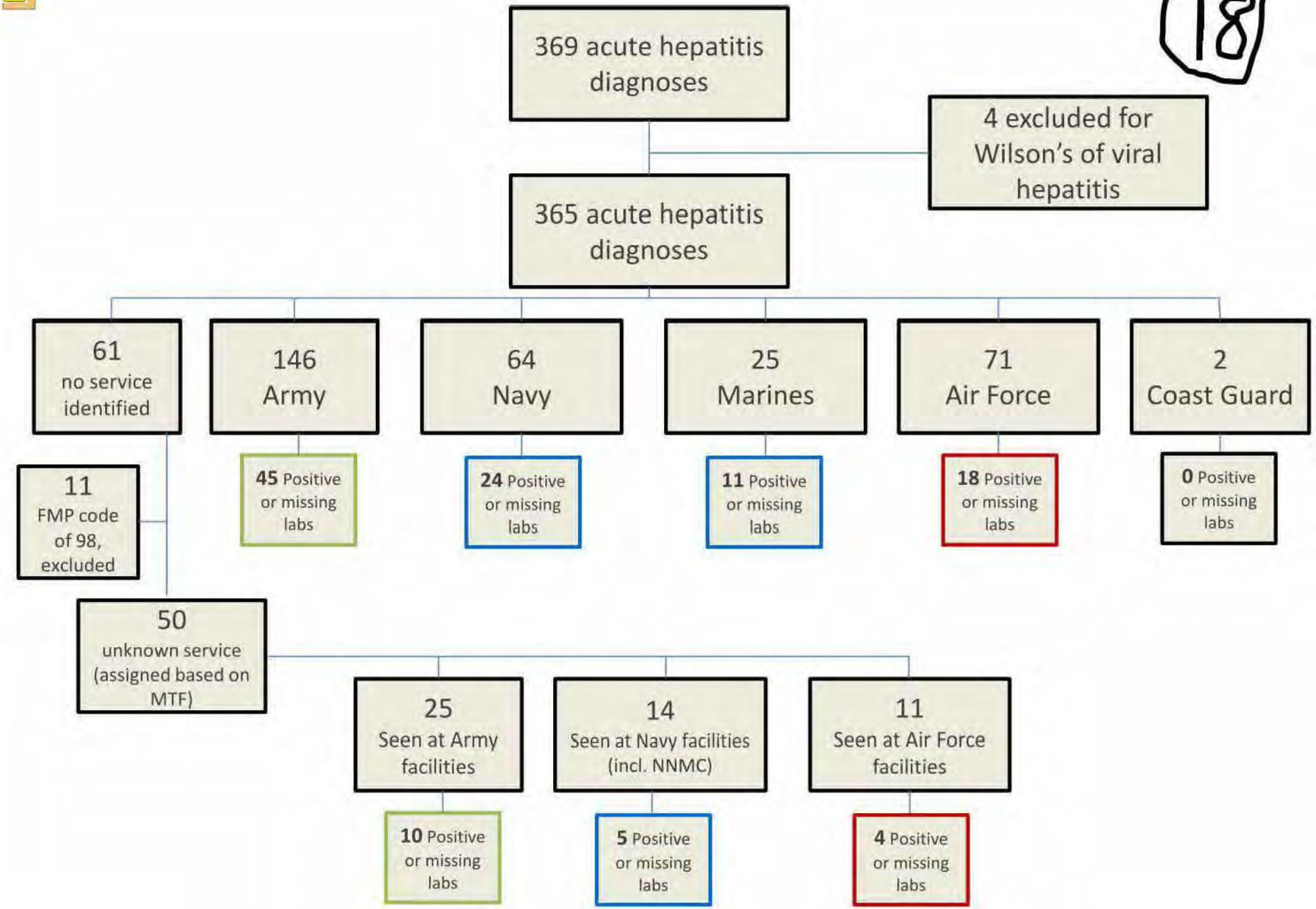
  Is intended for ingestion.

  Is not represented for use as a conventional food or as the sole item of a meal or diet.

  Is labeled as a "dietary supplement."

  Includes products such as an approved, new drug-certified antibiotic or licensed biologic that was marketed as a dietary supplement or food before approval, certification, or license (unless the Secretary of Health and Human Services waives this provision).

  Ref: DoDI 6130.05 http://www.dtic.mil/whs/directives/corres/pdf/613005p.pdf

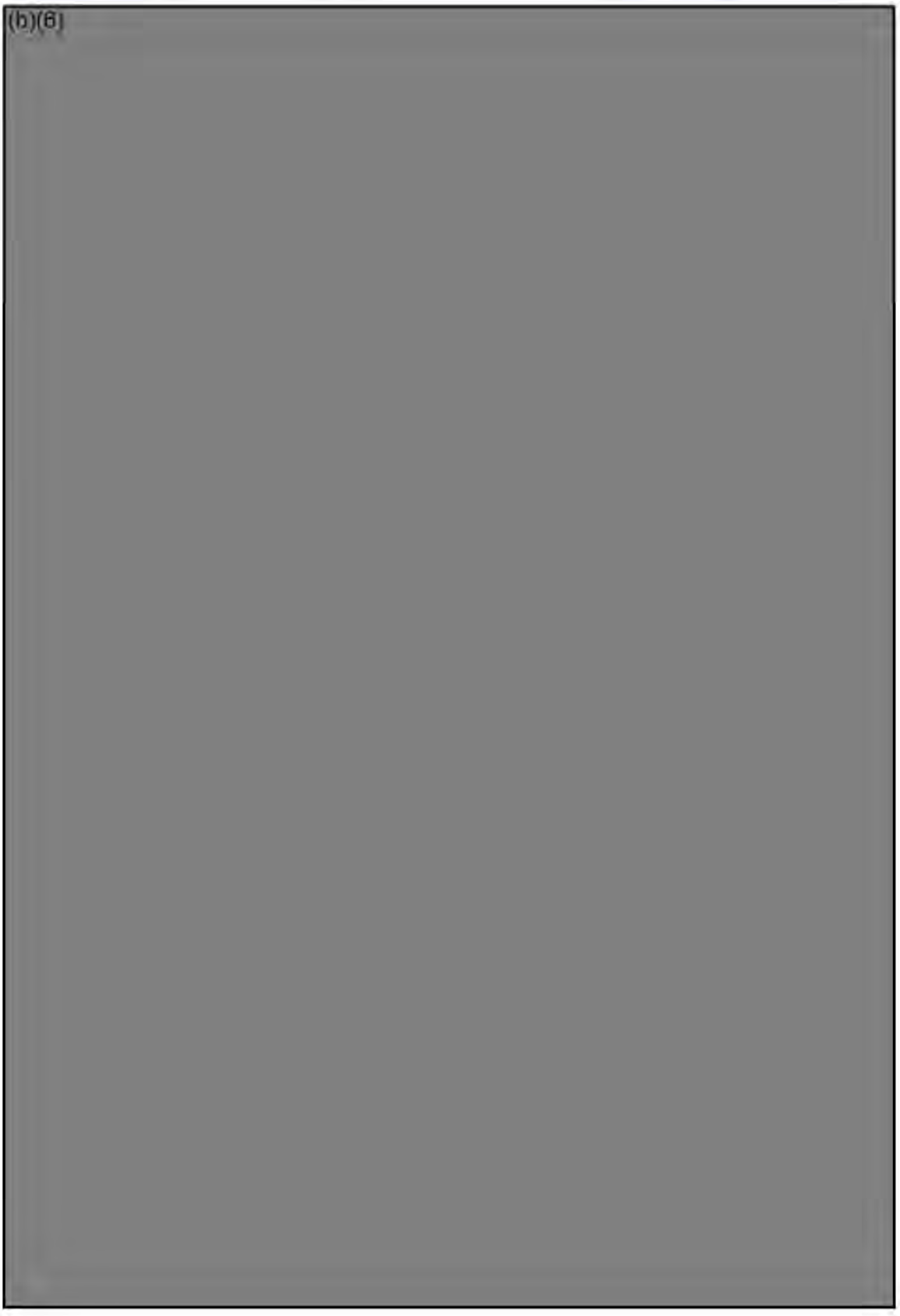

369 acute hepatitis diagnoses
4 excluded for Wilson's of viral hepatitis
365 acute hepatitis diagnoses
61 no service identified
146 Army
64 Navy
25 Marines
71 Air Force
2 Coast Guard
11 FMP code of 98, excluded
45 Positive or missing labs
24 Positive or missing labs
11 Positive or missing labs
18 Positive or missing labs
0 Positive or missing labs
50 unknown service (assigned based on MTF)
25 Seen at Army facilities
14 Seen at Navy facilities (incl. NNMC)
11 Seen at Air Force facilities
10 Positive or missing labs
5 Positive or missing labs
4 Positive or missing labs

19

Contact information Dietary Supplement Investigation

	Name Last	Name First	Rank/Title
CDC	(b)(6)		
			CAPT
			CDR/DoD Liaison
			Medical Officer/Tox
			Epidemiologist
			Research Officer
USAPHC			
			MAJ
			DR
			LTC
NMCPHC			
			CAPT
			DR
			Communicable Disease Epidemiologist
			LCDR
AFMSA			
			Col
USAFSAM			
			Col
			Lt Col
			MAJ
USCG			
			CAPT
AFHSC			
			CAPT
			CAPT
			LTC
			LCDR
			LCDR
DHA			DR
			COL
			DR (CTR)
CHAMP			
			DR

Work	Cell	Email Address
(b)(6)		

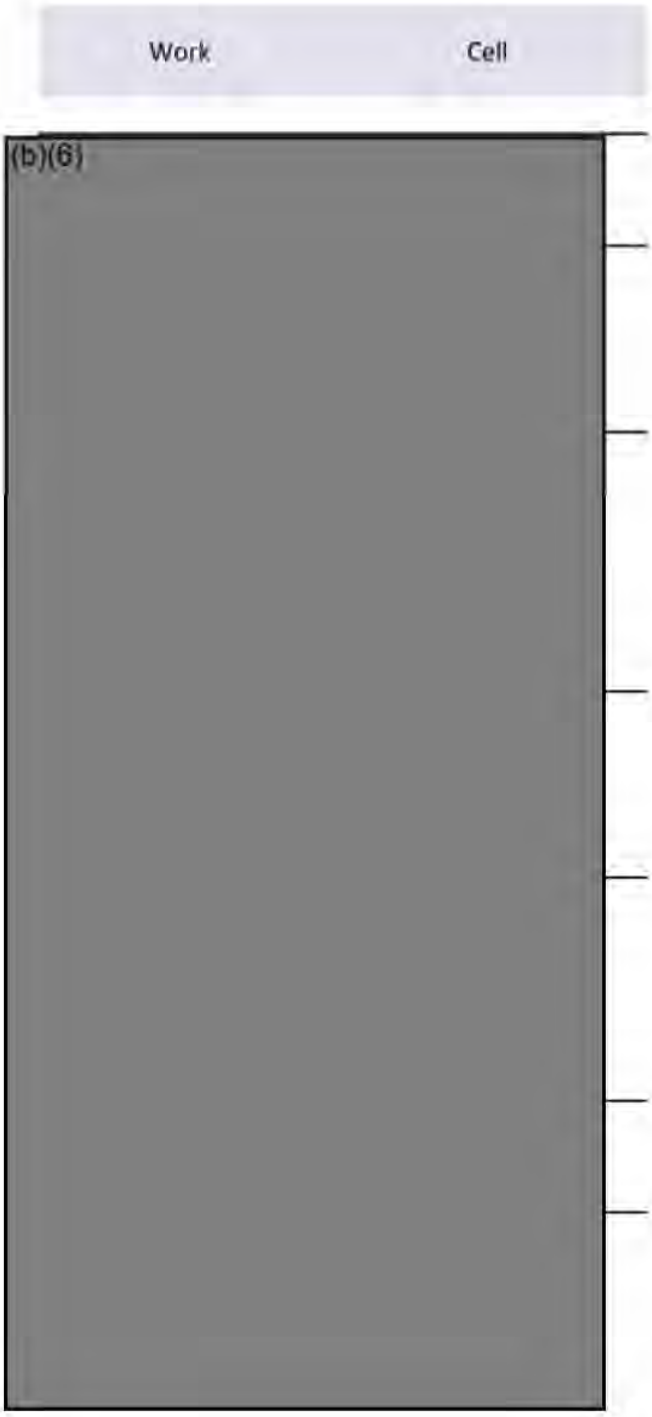


Notes

leading case ascertainment

Contact information Dietary Supplement Investigation

	Name Last	Name First	Rank/Title
CDC	(b)(6)		CAPT CDR/DoD Liaison
APHC			MAJ DR
NMCPHC			CAPT DR
USAFSAM			Col Lt Col Col MAJ
AFHSC			CAPT CAPT LTC LCDR
DHA			COL DR
HPRC			DR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(b)(6)

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FDA OxyELITE product guidance 14 Nov 2013

As discussed, our SMEs would like to receive the OxyELITE Pro products from patients identified by the DoD and Services. We request photographs of all sides/angles of product package (including bottom). Also provide the product description, and UPS tracking number for each product collected prior to shipment. Following your chain of custody procedures, please provide the collected samples to our Forensic Chemistry Center for analysis at the below address:

Mail to:
(b)(6) Ph.D.
Director
Forensic Chemistry Center, FDA
(b)(6)

Please email pictures and product information to "(b)(6) and (b)(6) "

For more information regarding the product recall please see,
http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm374395.htm

v/r,
(b)(6)
CORE Response Team 2
FDA/Office of Foods and Veterinary Medicine
(b)(6)
4300 River Road
College Park, MD 20740

(b)(6)

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From: (b)(6)
To:
Cc:
Subject: FW: FDA warning message for widest distribution
Date: Tuesday, October 15, 2013 10:04:31 AM

Sir/Ma'am,
Please ensure the widest distribution. If any members are currently using OxyElite Pro they are urged to stop its use while an investigation of possible links between the product and acute hepatitis cases are evaluated.
V/R,
(b)(6)

*****Best Viewed in HTML*****

Wing/MDG CC's and MAJCOM/SG's,

Sent on behalf of the Air Force Surgeon General Public Affairs Office:

Airmen urged to heed FDA warning about dietary supplement

The U.S. Food and Drug Administration is advising consumers to stop using OxyElite Pro, a dietary supplement, because of suspected links to acute hepatitis.

The FDA, along with the Centers for Disease Control and Prevention and the Hawaii Department of Health are investigating reports of acute non-viral hepatitis in Hawaii where 29 cases are linked to a dietary supplement.

The FDA urges consumers to stop using the product while the investigation continues. Distributed by USPlabs LLC in Dallas, Texas, the product is sold nationwide in retail stores and on the internet.

"We are urging Airmen to stop using the product until the investigation concludes and results are confirmed," said Col (b)(6) chief of Health Promotion, Air Force Medical Support Agency, Air Force Surgeon General.

There have been a total of 29 cases of acute non-viral hepatitis with an unknown cause reported in Hawaii. Eleven of the 29 patients have been

hospitalized with acute hepatitis, two have received liver transplants and one person has died. The CDC is also investigating other cases of liver injury nation-wide that could be related.

Symptoms of hepatitis include fever, fatigue, loss of appetite, nausea, vomiting, abdominal pain, dark urine, clay or gray-colored bowel movements, joint pain, yellow eyes, and jaundice.

Per Col (b)(6)

Airmen who are experiencing these symptoms should contact their health care provider immediately. Many Airmen reportedly use dietary supplements for weight loss or muscle building. In 2011, one-third of Airmen reported using legal bodybuilding supplements in the past year, including 15 percent in the last month.

We encourage Airmen to get educated on dietary supplement safety through Operation Supplement Safety, the Department of Defense dietary supplement education and safety campaign.

Information about the campaign is found at: www.hprc-online.org/opss. Visit this link for more information about the FDA warning: http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm370857.htm .

The AF SG POC is Col (b)(6) (b)(6) (DSN (b)(6) (b)(6)

(b)(6) DAF

Director, Commander's Action Group

Air Force Medical Operations Agency

(b)(6)

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From: [redacted]
To: [redacted]
Cc: [redacted]
Subject: Fwd: Dietary Supplement Manuscript Accepted
Date: Wednesday, December 07, 2016 8:48:03 PM

Emails
[redacted] PhD, MPH, FACSM
Professor and Director
Consortium for Health and Military Performance
A DoD Center of Excellence
Department of Military and Emergency Medicine
Uniformed Services University
4301 Jones Bridge Road
Bethesda, MD 20814
Office [redacted]
FAX [redacted]

Begin forwarded message:

From: [redacted]
Subject: Re: Dietary Supplement Manuscript Accepted
Date: June 27, 2016 at 10:33:25 AM EDT
To: [redacted]

Thanks much for the update! Congrats

[redacted]

[redacted] PhD, MPH, FACSM
Professor and Director
Consortium for Health and Military Performance
A DoD Center of Excellence
Department of Military and Emergency Medicine
Uniformed Services University
4301 Jones Bridge Road
Bethesda, MD 20814
Office [redacted]
FAX [redacted]

On Jun 27, 2016, at 9:03 AM, [redacted] wrote:

Hi all, our manuscript "Hepatotoxicity associated with weight loss or sports dietary supplements, including OxyELITE Pro™ — United States, 2013" was accepted to Drug Testing and Analysis over the weekend. I sincerely appreciate everyone's help throughout this process. I'll update everyone when I hear back about the publication

date.

Many thanks!
[redacted]

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This is an official

CDC HEALTH ADVISORY

Distributed via the CDC Health Alert Network
October 8, 2013, 2:30 ET (14:30 PM ET)
CDCHAN-00356

Acute Hepatitis and Liver Failure Following the Use of a Dietary Supplement Intended for Weight Loss or Muscle Building

Summary: *Recently, a number of previously healthy individuals developed acute hepatitis and sudden liver failure of unknown cause after using a dietary supplement for weight loss or muscle building. CDC recommends increased vigilance by public health agencies, emergency departments, and healthcare providers for patients who develop acute hepatitis or liver failure following use of a weight loss or muscle building nutritional supplement. CDC requests that state health departments report such occurrences to the CDC. CDC also recommends that, as part of a comprehensive evaluation, clinicians evaluating patients with acute hepatitis should ask about consumption of dietary supplements.*

Background:

On September 9, 2013, the Hawaii Department of Health (DOH) was notified of seven patients with severe acute hepatitis and sudden liver failure of unknown cause. The patients were previously healthy and sought medical care from May through September 2013. Clinicians reported that the seven patients had all used OxyELITE Pro, a dietary supplement marketed for weight loss and muscle gain, prior to illness onset.

The investigation is ongoing and the data presented are preliminary. Thus far, clinicians have reported 45 patients to the Hawaii DOH in response to a public health alert. Of those, 29 patients, including the original seven, were confirmed to have acute hepatitis after using a nutritional supplement for weight loss or muscle building. The median age of the 29 patients is 33 years; 14 (48%) are male. The date of the first reported laboratory test was used as a proxy for illness onset and ranged from May 10 through October 3, 2013. The most commonly reported symptoms included loss of appetite, light-colored stools, dark urine, and jaundice. Median laboratory values reported at the peak of illness were the following:

- aspartate aminotransferase (AST) 1,128 IU/L;
- alanine transaminase (ALT) 1,793 IU/L;
- alkaline phosphatase 150 IU/L; and
- total bilirubin 12.6 mg/dL.

Ten patients had liver biopsy data available at the time of this report. Seven had histology consistent with hepatitis from drug/toxic injury, with findings including hepatocellular necrosis and cholestasis. Three patients had liver biopsy findings of acute hepatitis associated with other etiologies such as autoimmune hepatitis. Eleven (38%) patients were hospitalized, with a median duration of seven days. One patient died, and two patients received liver transplants. Two remain hospitalized, and all other hospitalized patients have been discharged.

Of the 29 identified patients, 24 (83%) reported using OxyELITE Pro during the 60 days prior to illness onset. There was no other dietary supplement or medication use reported in common by more than two patients.

National case finding efforts have identified several individuals from states outside Hawaii with reported OxyELITE Pro or other weight loss or muscle building dietary supplement use prior to the development of

acute hepatitis of unknown cause. CDC, in collaboration with state health departments, is collecting additional clinical and epidemiologic information from these individuals to determine if this outbreak is national in scope.

Case definition:

An individual with acute-onset hepatitis of unknown etiology that developed symptoms on or after April 1, 2013 following use of a non-prescription weight loss or muscle building dietary supplement during the 60 days prior to illness onset.

With acute-onset hepatitis of unknown etiology defined as having BOTH:

- ALT $\geq$ 4 times the upper limit of normal
- Total bilirubin $\geq$ 2 times the upper limit of normal

AND

-negative workup for infectious or other explicative etiologies for hepatitis. Workup for other potential etiologies should include:

- Hepatic imaging (i.e., ultrasound/doppler, CT scan, MRI) not consistent with alternative, explicative etiologies
- Negative viral hepatitis panel
- No pre-existing diagnosis of chronic liver disease (e.g., autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, Wilson's disease, hemochromatosis)
- No recent hypotensive shock or septic episodes
- No history of alcoholism documented in medical records

Recommendations:

- Clinicians evaluating patients with acute hepatitis should ask about consumption of dietary supplements as part of a comprehensive evaluation.
- Clinicians should report patients meeting the case definition to the local or state health department, as well as the US Food and Drug Administration's MedWatch program online at https://www.accessdata.fda.gov/scripts/medwatch/ or by phone at 1-888-INFO-FDA.
- People who use dietary supplements for weight loss or muscle gain should do so with caution and under a medical provider's close supervision.

For more information:

State public health agencies should contact CDC at (866) 933-5295 if they identify patients who meet the case definition.

The Centers for Disease Control and Prevention (CDC) protects people's health and safety by preventing and controlling diseases and injuries; enhances health decisions by providing credible information on critical health issues; and promotes healthy living through strong partnerships with local, national, and international organizations.

Categories of Health Alert Network messages:

Health Alert	Requires immediate action or attention; highest level of importance
Health Advisory	May not require immediate action; provides important information for a specific incident or situation
Health Update	Unlikely to require immediate action; provides updated information regarding an incident or situation
HAN Info Service	Does not require immediate action; provides general public health information

##This message was distributed to state and local health officers, state and local epidemiologists, state and local laboratory directors, public information officers, HAN coordinators, and clinician organizations##

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EIS Update from Ireland 14 Nov 2013

Risk Assessment

Serious Public Health Impact

Yes. This is the first case to be reported in Ireland. However, as of 31 October 2013, the United States has reported 56 cases of acute non-viral hepatitis, including two cases of liver failure and one fatality, following the use of dietary supplements marketed for energy boost, muscle building, and weight loss.

Unusual or unexpected

Yes. The occurrence of the event itself is unusual for the population. The cause of liver illness in affected individuals has not yet been determined.

International disease spread

Yes. The affected product is on internet marketing sites. The dietary supplement is marketed in multiple countries. Information on international distribution of the affected product will be disseminated once available.

Interference with international travel or trade

Yes. The event resulted in requests for information by foreign officials and has gained media attention.

Date first Published to EIS:Thursday, November 14, 2013 - 21:49

List of published bulletins for event 2013-E000203

Details

On 13 November 2013, Ireland reported a case of non-viral hepatitis following the ingestion of OxyELITE Pro products, dietary supplements marketed for energy boost, muscle building, and weight loss. The Food Safety Authority Ireland (FSAI) and the Irish Medicines Board (IMB) has issued a joint warning not to purchase or consume certain food supplements, namely:

- OxyELITE Pro Super Thermo capsules;
- OxyELITE Pro Ultra-Intense Thermo capsules;
- OxyELITE Pro Super Thermo powder, and
- VERSA-1

The OxyELITE Pro range is associated with severe liver disorders, including hepatitis and liver failure, with one case reported in Ireland to date. The case consumed OxyElite Pro after purchasing it online.

Both OxyElite Pro and VERSA-1 are produced by USP Labs LLC in the USA. Although VERSA-1 has not been associated with liver disease, both it and OxyElite Pro contain the ingredient aegeline, which cannot be excluded as a cause of illness. The OxyElite Pro products were on retail sale in Ireland.

Retailers have been requested to remove the products from sale.

The FSAI press release containing full details is available online:
http://www.fsai.ie/news_centre/food_alerts/oxyelite_warning.html
<http://www.fsai.ie/news_centre/food_alerts/oxyelite_warning.html>

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Statement on Use of Dietary Supplements and Acute Hepatitis Illness

The Department of Defense is advising all Service members and their families to follow Centers for Disease Control and Prevention (CDC) and Food and Drug Administration (FDA) guidance to stop using any dietary supplement labeled OxyELITE Pro and VERSA-1. The Department is participating in an investigation with the CDC, FDA and Hawaii Department of Health on the acute hepatitis and liver failure of individuals who may have taken these dietary supplements. As a precaution, the Department has ordered the removal of all OxyELITE Pro and VERSA-1 products from military facilities.

Service members and their families who believe they have been harmed by the use of this product should contact their health care provider. Health care providers are asked to report any adverse events related to the use of OxyELITE Pro and VERSA-1 to the FDA's MedWatch Safety Information and Adverse Reporting Program at www.fda.gov/MedWatch/report.htm .

FDA Guidance: http://www.fda.gov/Food/RecallsOutbreaksEmergencies/Outbreaks/ucm370849.htm

CDC Guidance:
http://emergency.cdc.gov/HAN/han00356.asp

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Case #	OEP + other Supplement	OEP	Total # Supplements
1	Yes	Yes	2
2	No	Yes	1
3	No	No	3
4	Yes	Yes	2
5	Yes	Yes	2
6	No	No	1
7	No	No	1
8	No	No	2
9	No	Yes	1
10	No	No	3
11	No	Yes	1
12	No	No	1
13	No	No	1
14	No	No	1
15	No	No	1
16	No	No	1
17	No	Yes (> 6 mos ago)	1
18	Yes	Yes	8
19	Yes	Yes	1
20	Yes	Yes	3
21	Yes	Yes	2
22			
23	No	No	3
24	No	Yes	1
25	No	Yes	1
26			
27	No	No	1
28	Yes	Yes	3
29	Yes	Yes	3
30	Yes	Yes	5
31			
32			

Other Supplement

Vita Pak
No
C4, No Explode, Whey Protein
Xenadrine
BCAA
Monster Energy Drink (20 oz.) 3 drinks a day
True-Slim Tea
EAS Lean 15 Protein Powder, EAS 100% Whey Protein
No
6 Sar Pro Nutrition MuscleTech,BFN testosterone booster, MuscleTech NAO vapor (pre-workout)
No
C4 pre-workout
CRAZE
E-strength
No Xplode
Cellucor Super HD
Jack 3D
Hyper Shred, Super Pump Max, No Xplode, Jack 3D, 1 MR, Pump HD, Bull Knox
No
Colon RX-MEGAHO NUTRITION, GNC Herbal Plus Standardized (Fenugreek)
Epistane
waiting on questionnaire still
Monster Drinks, Mountain Dew Energy Drink, Atro-Phex pills
No
No
Refused to Participate - no questionnaire
C4
Multivitamins, amino acid pills?
CLA and L-carnitine
Whey Protein, Creatine monohydrate, L-arginine, Roxylean

Refused to Participate - no questionnaire
Refused to Participate - no questionnaire

How long?	Case Status
	Suspect
	Suspect
	Suspect
	Suspect
	Probable
	Not Case?
	Probable
	Probable
	Probable
	Probable
	Probable
1 year	Probable
	Probable
doesn't know	Probable
couple months	Probable
consistently takes	suspect
1 mos; and > 6 mos	Probable
2 weeks OEP, approx 2 mos for Hypershred (and others?)	Probable
	Suspect
	Probable
	Probable
	Probable
	Suspect
	Probable
	Probable
	Probable
	Probable
	Probable
approx 1 year	Probable
	Probable
	Suspect
	Probable

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Recently, a number of previously healthy individuals developed acute hepatitis and sudden liver failure of unknown cause after using a dietary supplement for weight loss or muscle building. Nationwide, the Hawaii state department of health and the Centers for Disease Control and Prevention report a total of 69 confirmed cases of supplement-associated acute hepatitis and liver failure. The Armed Forces Health Surveillance Center, along with the US Army Public Health Center and the other Service public health centers, is investigating potential cases within the Department of Defense (DoD) Active Duty population and also among other beneficiaries. The majority of cases have been linked to OxyElite Pro dietary supplement products from USPLabs. Recalled supplements have been pulled from store shelves on base. Service Members should be reminded that dietary supplements are not regulated by the FDA, and should be used with caution. Unlike drug products, there are no provisions in the law for the FDA to "approve" dietary supplements for safety or effectiveness before they reach the consumer. More information on dietary supplements and their use within the DoD is available at: http://hprc-online.org/dietary-supplements. For further information, please contact AFHSC at: (b)(6) (b)(6)