EMERGENCY USE AUTHORIZATION: AT ZERO HOUR

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REVIEW ARTICLE

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ABSTRACT

The Emergency Use Authorisation (EUA) authority plays a vital role in US FDA. They provide the authority/permission to use the unregistered products/registered product with unregistered route to treat the life threatening damages to the patients in world in some emergency conditions. The aim of this work is to give an overview on EUA in life threatening conditions and there challenges in getting the permissions under regulations with example of E-bola virus. The e-bola is a virus. It is a hemorrhagic fever deadly disease caused by one of the E-bola viral strain, which is wide spread in West Africa. The -Secretary of the Department of homeland security (DHS), determined, pursuant to section 319F-2 of the Public Health Service Act, that the Ebola virus presents a material threat against the United States population sufficient to affect national security. Issuance of EUA by the FDA Commissioner requires several steps under section 564 of the FD&C Act. The FDA Commissioner, can only issue the EUA, if criteria for issuance under the statute are met. This study's highlights the importance of the EUA in emergency when there is no medicine for disease/virus in the world. For example the FDA has issued a EUA to use the ReEBOV which is the Rapid Antigen Test device designed by Lusys lab co. Pvt. Ltd. for detecting the Zaire Ebola virus.

Keywords: Emergency authorisation, Zaire Ebola virus, ReEBOV, Unregistered product.

INTRODUCTION

The emergency use authorisation authority plats a vital role in US FDA. They provide the authority/permission to use the unregistered products /registered product with unregistered route to treat the life threatening damages to the patients in world in some emergency conditions with some of the special specified agents.

Section 564 of federal food, drug & cosmetics act issues permission for such product to diagnose, treat, prevent serious conditions caused by the biologics, chemicals, radiological or nuclear agents, if certain statuary ;criteria are met. The secretary of the department of HHS has powers to issue or refuse the EUA under section 564 of FD&C act to the FDA commissioner.

This article is been done using the material from the regulatory authority website, review articles & public domain.

- US FDA,
- EUA/EMA &
- Nordic-Bavarian.

Basis for issue of an EUA by FDA

Once the HHS Secretary has declared an emergency justifying the emergency use, the FDA Commissioner can authorize an emergency use only if, after consultation with the national institute of health (NIH) and the Centers for Disease Control and Prevention (CDCP), the Commissioner determines that certain statutory criteria have been met. Particularly, the Commissioner must wind up, as follows:

1. The agent specified in the declaration of emergency can cause a serious or life-threatening disease or condition.
2. Based on the scientific evidence available, it is reasonable to believe that product may be effective in diagnosing, treating, or preventing—
   (a) The serious or life-threatening disease or condition, or
   (b) A serious condition caused by a product authorized under section 564, or approved, cleared, or licensed under the PHS Act, for diagnosing, treating, or preventing the disease or condition.

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3. There is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating such serious or life-threatening disease or condition.
4. On reporting the adverse events or side effects.

An EUA may remain in effect for up to 1 year based on the HHS declaration mitigating the emergency use, unless such declaration is terminated or the EUA is revoked (e.g., if the criteria for issuance of the authorization are no longer met or other circumstances make revocation appropriate to protect the public health or safety) before 1 year. After 1 year, both the declaration of an emergency and EUAs issued under that declaration may be renewed, if justified. The law requires FDA to publish in the Federal Register a notice that announces each EUA and termination or revocation of an authorization and that provides an explanation of the reasons for the action. (1)

Reporting the Adverse events

Health care professionals who observe & experience adverse events, side effect or medication errors will report to MedWatch by:

- Submitting a MedWatch Form 3500 or
- Calling 1-800-FDA-1088.

While reporting to MedWatch for EUA's adverse events or medication errors. The report should include that the product was used under a EUA by including in the description of event section (Section B.5) of the MedWatch, Form 3500, the abbreviations "EUA" or the words "Emergency Use Authorization."

Process for issuance of the EUA

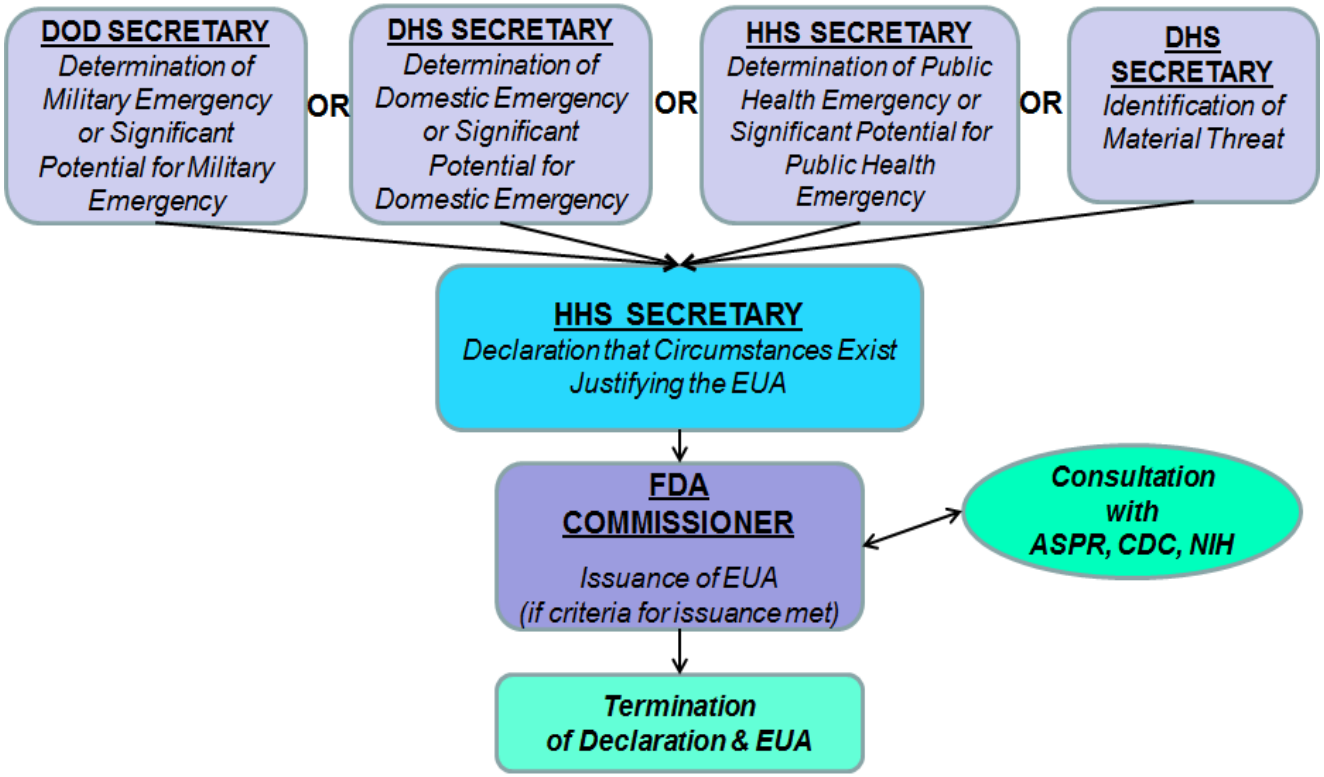

Figure 1: Process for issuance of the EUA

Issuance of an EUA by the FDA Commissioner requires several steps under section 564 of the FD&C Act. First, one of the four following determinations must be in place:

The Department of Defense (DOD) Secretary issues a determination of military emergency or significant potential for military emergency

The Department of Homeland Security (DHS) Secretary issues a determination of domestic emergency or significant potential for domestic emergency.

The Department of Health and Human Services (HHS) Secretary issues a determination of public health emergency or significant potential for public health emergency

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The DHS Secretary issues a material threat determination

After one of the above four determinations is in place, the HHS Secretary can issue a declaration that circumstances exist to justify issuing the EUA. This declaration is specific to EUAs and is not linked to other types of emergency declarations.

The FDA Commissioner, in consultation with the HHS, CDCP, and the NIH, can then issue the EUA, Assistant Secretary for Preparedness and Response (ASPR), if criteria for issuance under the statute are met. FDA publishes public notice of each EUA that is issued in the Federal Register.

The last step in the process is termination of declaration and EUA, if appropriate and needed. (2)

FDA issued the EUA for Medical device for E-Bola

E –Bola is the virus got originated in West Africa in 2014 and has affected more than 50,000 citizens in West Africa. Thus USA as the developed country is trying to find out the causative organism for this deadly disease/ disorder and has issued the EUA for the latest medical devices discovered by the US government agencies.

On September 22, 2006, then-Secretary of the Department of Homeland Security (DHS), Michael Chertoff, determined, pursuant to section 319F-2 of the Public Health Service (PHS) Act (42 U.S.C. § 247d-6b), that the Ebola virus presents a material threat against the United States population sufficient to affect national security. Pursuant to section 564(b)(1) of the Act (21 U.S.C. § 360bbb-3(b)(1)), and on the basis of such determination, the Secretary of HHS declared on August 5, 2014, that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection of Ebola virus, subject to the terms of any authorization issued under 21 U.S.C. § 360bbb-3(a). (3)

Ebola, previously known as Ebola hemorrhagic fever, is a rare and deadly disease caused by infection with one of the Ebola virus species. Ebola can cause disease in humans and nonhuman primates (monkeys, gorillas, and chimpanzees). Ebola is caused by infection with a virus of the family Filoviridae, genus Ebola virus. Ebola was first discovered in 1976 near the Ebola River in what is now the Democratic Republic of the Congo. Since then, outbreaks have appeared sporadically in Africa. The natural reservoir host of Ebola virus remains unknown. However, on the basis of evidence and the nature of similar viruses, researchers believe that the virus is animal-borne and that bats are the most likely reservoir. Four of the five virus strains occur in an animal host native to Africa. People get Ebola through direct contact. (Through broken skin or mucous membranes in, for example, the eyes, nose, or mouth) (4)

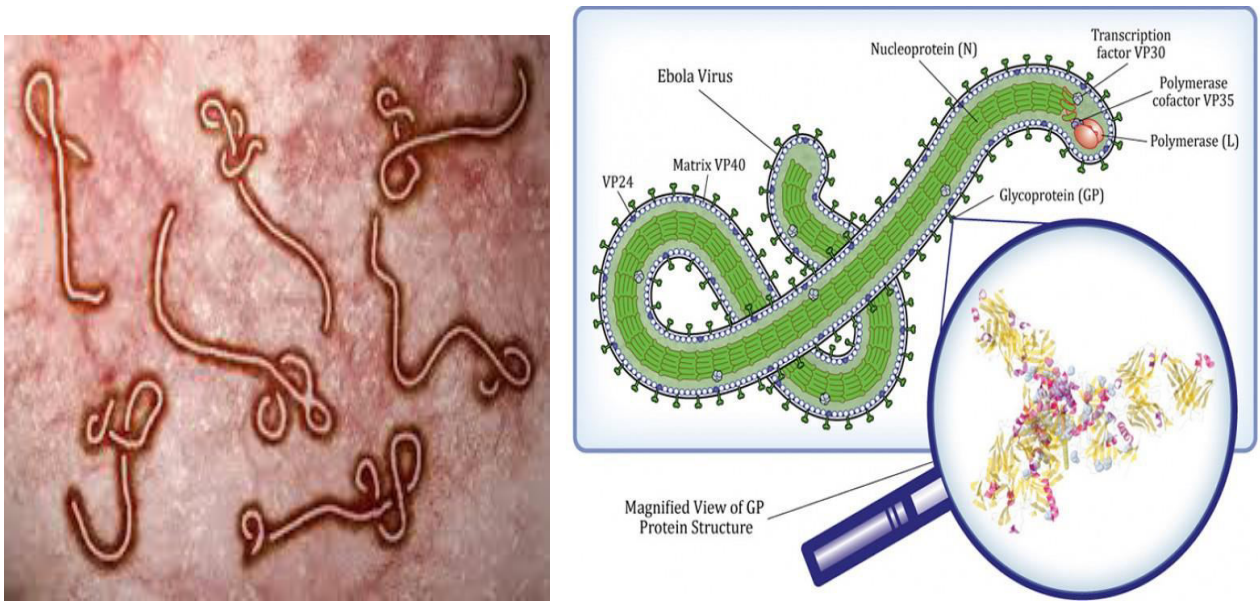

Figure 2: The microscopic picture of E-BOLA virus and the detailed structure of E-BOLA (5)

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This are the medical devices got the EUA by the US FDA for the diagnosis of the E-Bola virus in West Africa. Thus the American health care companies are discovering the new medical devices for the diagnoses for the virus and were successful in figuring out the structure of the virus which causes E-Bola. (6)

EZ1 Real-time RT-PCR Assay → takes time from hours to days to give the results. While,

OraQuick® Ebola Rapid Antigen Test → gives the results within minutes to hours. (3)

Table 1: Medical Devices got EUA by US FDA in last 2 years for E-Bola

Medical product	EUA determination & declaration.	Name of the agency.	Date of issuance of EUA.
EZ1 Real-time RT-PCR Assay kit.	Declaration Regarding Emergency Use of in vitro Diagnostics for Detection of Ebola Virus	Department of defence	October 10, 2014
CDC Ebola Virus VP40 Real-time RT-PCR Assay kit.	Declaration Regarding Emergency Use of In Vitro Diagnostics for Detection of Ebola Virus	Center for disease control & prevention	October 10, 201
LightMix® Ebola Zaire rRT-PCR Test kit.	Declaration Regarding Emergency Use of In Vitro Diagnostics for Detection of Ebola Virus	Roche Molecular Systems, Inc.	December 23, 2014
ReEBOV™ Antigen Rapid Test kit.	Declaration Regarding Emergency Use of In Vitro Diagnostics for Detection of Ebola Virus	Corgenix, Inc.	February 24, 2015
OraQuick® Ebola Rapid Antigen Test kit.	Declaration Regarding Emergency Use of In Vitro Diagnostics for Detection of Ebola Virus	(OraSure Technologies, Inc.)	July 31, 2015

EUA issued for emergency drugs or vaccines:

US FDA has issued numerous EUAs. Many EUAs were issued in response to the 2009 H1N1 influenza pandemic. Some of the examples are as follows:

Table 2: EUA issued in response to the 2009 H1N1 influenza pandemic

Emergency	Products Authorized	Rationale	Date
Bacillus anthraci	Declaration That Circumstances Exist Justifying Authorization of Emergency Use of All Oral Formulations of Doxycycline Accompanied by Emergency Use Information	The Secretary of HHS is declaring that circumstances exist justifying the authorization of emergency use of all oral formulations of doxycycline accompanied by emergency use information subject to the terms of any authorization issued by the Commissioner of Food and Drugs under section 564(a) of the FD&C Act.	7/23/2013

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Middle East respiratory syndrome Coronavirus (MERS-CoV)	CDC Novel Coronavirus 2012 Real-time RT-PCR Assay	On May 29, 2013 Secretary Kathleen Sebelius determined that Middle East respiratory syndrome coronavirus (MERS-CoV) poses a significant potential for a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad. On the basis of this determination the Secretary declared that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection of the Middle East respiratory syndrome coronavirus (MERS-CoV).*	7/5/2013
H7N9 Influenza	CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay	On April 19, 2013 Secretary Kathleen Sebelius determined that avian influenza A (H7N9) poses a significant potential for a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad. On the basis of this determination the Secretary declared that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection of the avian influenza A(H7N9) virus	4/22/2013
Bacillus anthracis	Renewal of Declaration Regarding Emergency Use of Doxycycline Hyclate Tablets Accompanied by Emergency Use Information	The Secretary of HHS is renewing her July 20, 2011 declaration of an emergency justifying the authorization of emergency use of all oral formulations of doxycycline accompanied by emergency use information subject to the terms of any authorization issued by the Commissioner of Food and Drugs under 21 U.S.C.	6/28/2012

Thus according to the PHS act there are many more EUA issued for the emergency conditions by FDA in USA for the protection of the public health. (7)

Limits on the use of EUA product

For unapproved products, the law requires that certain conditions to be established by the FDA Commissioner on an EUA: that the Commissioner finds right to protect the public health, and permits the Commissioner to establish other conditions that he finds necessary or appropriate to protect the public health. Such conditions may include a requirement to disseminate information to health care professionals or authorized dispensers and to

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prospective patients and other consumers regarding the EUA, the product's significant known and potential benefits and risks, and the extent to which such benefits and risks are unknown. Other conditions may include adverse event reporting and monitoring, data collection and analysis, and recordkeeping and records access.

For unapproved uses of approved products, certain of these conditions and other conditions may be required in a EUA.

Use of a product in EUA condition must be consistent or reliable with any conditions imposed on the EUA under the public health service (PHS) act. (1,7)

CONCLUSION

If there was no medicine to treat the disease E-Bola with any authority of any country in world then US FDA gave permission of EUA. In 2014, permission for the use of vaccines and some diagnostic kits for diagnose of E-bola virus & use of the vaccine for the INDA was permitted for the clinical trial I, II and III in West Africa and other country for preventing the spreading & diagnoses for the causative organism.

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CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest.

REFERENCES

1. Emergency Use Authorization for Oral Formulations of Doxycycline for Post Exposure Prophylaxis of Inhalational Anthrax [Internet]. FDA; 2005 [cited 2015 Oct 11]. Available from: http://www.fda.gov/EmergencyPreparedness/Counterterrorism/ucm269226.htm
2. Summary of Process for EUA Issuance, Issuance EUA. [Internet]. FDA; 2015 [cited 2015 Oct 13]. Available from: http://www.fda.gov/emergencypreparedness/counterterrorism/medicalcountermeasures/mcmlegalregulatoryandpolicyframework/ucm411445.htm
3. Lewis S. Bavarian nordic announces that the oxford vaccines group has initiated a phase 2 study of the ebola prime-boost vaccine regimen combining mva- bn ® filo and janssen' s advac ® technology [Internet]. Bavarian Nordic; 2015 [cited 2015 Oct 03]. Available from: http://www.bavarian-nordic.com/investor/news/news.aspx?news=4491
4. Centers for Disease Control and Prevention (CDC), About Ebola virus disease [Internet]. CDC; 2014 [cited 2015 Oct 12]. Available from: http://www.cdc.gov/vhf/ebola/about.html
5. e bola virus pics Google Search [Internet]. Google; 2015 [cited 2015 Nov 26]. Available from: https://www.google.co.in/search?q=e+bola+virus+pics&espv=2&biw=1242&bih=566&source=lnms&tbm=isch&sa=X&ved=0CAYQ_AUoAWoVChMIj_DYt77syAIVBuKmCh0qLwho
6. Emergency Use Authorization MCM Legal, Regulatory and Policy Framework, Emergency Use Authorization [Internet]. FDA; 2015 [cited 2015 Oct 16]. Available from: http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm182568.htm#cepheid
7. Emergency Use Authorization (EUA) All Items All Items [Internet]. U.S Department of Health and Human Services; 2015 [cited 2015 Oct 03]. Available from: http://www.phe.gov/emergency/news/healthactions/Lists/EUA/AllItems.aspx

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