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# Review and Comparison of the US FDA and the UK MHRA on Good Manufacturing Practice (GMP) Implementation

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**ABSTRACT**

A government is responsible for ensuring public health and safety. One of the approaches is to establish a regulatory body that governs health-related items such as pharmaceuticals and other human health-related products. These regulatory bodies exist to ensure that goods satisfy high standards of quality, safety, and efficacy. This article investigates several aspects of regulatory bodies' regulation and Good Manufacturing Practice (GMP) standards controlled by two regulatory organizations, the Food and Drug Administration (FDA) and the Medicines and Healthcare products Regulatory Agency (MHRA). Both regulatory agencies appear to have some items controlled and fairly specific product authorization guidelines. It is apparent that both regulatory authorities have some comparable notions in common when it comes to GMP implementation, product registration, mutual recognition agreements, and MoU implementation.
**Keywords:** FDA; MHRA; GMP; regulatory agency

## INTRODUCTION

A government should ensure their citizens and residents at their greatest health condition. For fulfilling this goal, a country may allocate a special proportion of its budget and priority to developing and maintaining a high standard of health conditions such as by setting and organizing a robust health system (Feldmann & Muller, 2012). One of the health systems which may support this vision is by organizing a special agency or regulatory body which specifically regulates products related to human health such as medicines, food, and medical devices. The regulatory body then should responsible for ensuring the related products meets the quality, safety, and efficacy requirements.

Based on the regulations required by Good Manufacturing Practice (GMP) principles, high standards of pharmaceutical products should be built, developed, and designed from the production planning, the product manufacturing, and distribution, until it is given to the consumer. The product manufacturer particularly pharmaceutical manufacturers in every country around the globe should maintain a high standard of GMP implementation based on the regulation or guidelines generated from their national agency guidelines, adopted, or referred regulatory guidelines, or international guidelines (Gouveia et al., 2015). It can be seen from several regulatory bodies and pharmaceutical stakeholders around the world have agreed to harmonize GMP guidelines that can be used in certain agreed-upon countries. Pharmaceutical Inspection Co-Operation Scheme (PIC/S), The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), World Health Organization (WHO) GMP Guidelines, and Eudralex by the European Commission are examples of globally approved harmonization.

The US Food and Drug Administration (FDA) is one of the most impactful regulatory authorities in the world as it has a huge market for both produced products for US consumption and export products. It may be seen as some countries throughout the world follow FDA statutes and refer to them for national direction on food and drug control. Besides that, the FDA, which roles under the US Department of Health and Human Services does not only regulate pharmaceutical manufacturer operations ensuring the quality, safety, and efficacy of human and veterinary pharmaceuticals, but also medical devices, biological products, food supply, cosmetics, and radiation products (FDA, 2022).

The other regulatory agency which likely has a major impact on the world is the UK Medicines and Healthcare products Regulatory Agency (MHRA) which is a part of the UK Department of Health and Social Care. It may be caused by some major pharmaceutical companies having their manufacturing facility

**Table I. Comparison of Product Regulated by US FDA and UK MHRA**

| US FDA | UK MHRA |
|---|---|
| - Food<br>- Drugs<br>- Medical devices<br>- Radiation-emitting products<br>- Vaccines, blood, and biologics<br>- Animal and veterinary<br>- Cosmetics<br>- Tobacco products | - Medicines<br>- Medical devices<br>- Blood components and products<br>- Tobacco products<br>- Vaccines |

and headquarter in the UK such as GlaxoSmithKline and AstraZeneca which distributes their product across the globe. Both regulatory agencies may have their regulation related to Good Manufacturing Practice (GMP) to be implemented by the market. This article will review and compare some critical aspects related to the pharmaceutical product on two regulatory agencies (US FDA and UK MHRA).

## METHODOLOGY

This article will examine the information from the US Food Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA) websites and some supporting publications about both regulatory overview and comparison in particular on the scope of work, implementation of GMP regulation, pharmaceutical product approval, MRA, and MoU agreement.

## RESULT AND DISCUSSION

### Scope of Regulated Products

The food and Drug Administration (FDA) and the Medicines and Healthcare Products Regulatory Agency (MHRA) are likely to regulate similar product scope. From the official website, FDA classifies the regulated are food, drugs, medical devices, radiation-emitting products, vaccines, blood and biologics, animal and veterinary, cosmetics, and tobacco products (FDA, 2022). These products are likely to have a similar scope as the MHRA does. This UK regulatory body is responsible for regulating medicines, medical devices, blood components, blood products, tobacco products, and vaccines (MHRA, 2022). Despite using different terms used on drugs and medicines, both regulatory bodies are responsible for controlling drugs or medicine, medical devices, and vaccines including blood products and biologics.

Besides, FDA also enforces guidance and regulation for food products and cosmetics. The agency provides detailed guidelines and resources through the FDA website from product registration, production, distribution, and research related. The information and guidance are provided for all related stakeholders such as industry, consumers, and health professionals. On the other side, different from the US FDA, the UK MHRA does not cover food as this sector is regulated by the UK Foods Standard Agency, while cosmetics in the UK are regulated by the Cosmetics, Toiletry, and Perfumery Association (CTPA).

Furthermore, FDA rules for veterinary medicines are described thoroughly on the US FDA website for any veterinary products including animal drugs, animal medical devices, animal food, and guidance for industry and veterinarians. Different from the US FDA, veterinary medicines in the UK are governed by the Veterinary Medicines Directorate under the Department of Environment, Food, and Rural Affairs. This condition is similar to radiation products and services. While it is covered by FDA in the US, Public Health England (PHE) Centre for Radiation, Chemical, and Environmental Hazards is responsible for its implementation in the UK.

### Good Manufacturing Practice (GMP) Implementation in the Impacting Countries

The pharmaceutical sector should use Good Manufacturing Practice (GMP) principles to assure product quality, however the criteria that must be followed vary by nation based on the legal status of GMP guidelines applied in a related field. It is most likely due to the fact that certain nations implement their national GMP standards as required legislation that must be followed by the pharmaceutical industry and all

**Table II. Related parts on 21 CFR by US FDA**

| Part of 21 CFR | Description |
|---|---|
| 21 CFR Part 314 | FDA approval to market a new drug devices |
| 21 CFR Part 210 | cGMP in Manufacturing Processing, packing or holding of Drugs |
| 21 CFR Part 211 | cGMP for Finished Pharmaceuticals |
| 21 CFR Part 212 | cGMP for Positron Emission Tomography Drugs |
| 21 CFR Part 600 | Biological Products: general |

pharmaceutical-related industries. It can be seen from the different implementations on both the UK MHRA and the US FDA. The UK Medicines and Healthcare Products Regulatory Agency (MHRA) sets the least standard of Good Manufacturing Practices (GMP) for manufacturer license holders, wholesale license holders, blood establishment authorization holders, and non-UK sites employed by UK MA holders by referring to the GMP guidance which is published together by MHRA and European Medicines Agency (EMA) (MHRA, 2020).

For regulatory implementation, EMA applies a decentralized system that allows national authorities in each country to define their procedures for their internal process. MHRA and EMA administer GMP requirements under EudraLex Volume 4 Good Manufacturing Practice (GMP) guidelines (European Commission, 2022), besides utilizing the Orange Guide for pharmaceutical manufacturers and distributors too. Thus, even though it is not part of EU countries and has its own regulatory body, the UK still refers to the GMP guideline which was agreed upon by EU-MHRA to be implemented.

On the other side, the US Food and Drug Administration (FDA) seems that it set its guidance and regulation related to Good Manufacturing Practice (GMP) on pharmaceutical products. It can be seen in their robust and detailed Code of Federal Regulation (CFR) which is publicly shared on its specific and regularly updated website. The pharmaceutical drug product quality regulation is detailed in some parts in CFR Title 21 which is interpreted from Federal Food, Drug, and Cosmetic Act and some related regulations where (FDA, 2022).

In addition, as the product scope in the US FDA is larger than the UK MHRA, the GMP regulation detailed by this agency also details the implementation on other products such as food and dietary supplements, cosmetics, and food for animals. Similar to cGMP on drugs, these guidelines are implemented to ensure product safety which details the hygienic practice, facility and plant equipment, production, and process control (FDA, 2022). The deviation from these guidelines may cause the products deemed adulterated or misbranded.

**Pharmaceutical Product Registration and Evaluation Process**

A regulatory body must establish a detailed process and guidelines for product approval and its evaluation process. The US FDA implements a registration and evaluation process based on the Code of Federal Regulations (CFR) Title 21 part 314 about applications for FDA approval to market a new drug. It can be seen from the CFR website that the FDA details and describes all the required documents and activities which should be fulfilled by the applicants who registered their drug products. There are five application types defined by the FDA. These are Investigational New Drug (IND) application, New Drug Application (NDA), Abbreviated New Drug Application (ANDA), Therapeutic Biologics Applications (BLA), and Drug Applications for Over-the-Counter (OTC) Drugs. Those application types define the application process, requirements, and guidance on several supporting CFR sections which describes on the CFR website. In addition, the US FDA registration process needs to be supported by some essential data such as chemistry, manufacturing and control information, nonclinical, clinical, bioequivalence data, and patent information. Furthermore, the US FDA allows for amendments for any unapproved new drug applications based on the result of the review. The applications also may be needed for supplements or resubmission to be granted.

On the other hand, the UK MHRA categorize product license application into two different routes: national and international

routes. This agency utilizes an electronic Common Technical Document (eCTD) for pharmaceutical product applications. This agency also relies on the European Commission for the approval of the new drug for the centralized procedure. EMA regulatory body applies two pathways to register medicine (European Medicines Agency, 2022). Those are the Centralised Route and National Route. The centralized method allows the UK MHRA to award product registration after the European Union has approved it. This technique is required for all novel substances for HIV/AIDS, cancer, diabetes, neurodegenerative illnesses, auto-immune or other immune diseases, viral disease, biotechnology processed medication, orphan medicine, advance-therapy medicine, and veterinary medicine for growth. The national route allows a member country to license medication and is applicable for items that were authorized before the founding of the EMA or that are not in the scope of the centralized procedure.

Furthermore, the UK MHRA may issue product registration (marketing authorization) that has been authorized in other EU member countries via a decentralized and mutual recognition process. It is because the EMA has these guidelines, pharma companies that expand their product to other EU companies and not in a centralized scope may use decentralized procedures and mutual-recognition procedures in which marketing authorization from one EU member can be accepted in another or several EU member states (MHRA, 2021). Thus, it seems that the implementation of the registration process on MHRA and FDA may differ on the regulatory body reference procedure. It can be seen from the discussion above that MHRA implement its regulatory scheme and also refers to European Commission which is detailed by EMA. On the other side, the US FDA has its regulatory guideline for product approval on 21 CFR details.

**Memorandum of Understanding (MoU) and Mutual Recognition Agreement (MRA)**

A Memorandum of Understanding (MoU) may bring an effective collaboration of regulatory bodies with other parties. It is because this collaboration scheme may enable regulatory bodies to share initiatives or information and facilitation (MHRA, 2016). The UK MHRA has some MoU with its counterparts such as with Swissmedic (Switzerland) and Central Drugs Standard Control Organisation (CDSCO - India). With India's CDSCO, the UK MHRA shares information and opportunities for technical cooperation as MHRA assessors perform Indian manufacturing sites for UK medicines supply from India (MHRA, 2015). It is similarly implemented in the US where the FDA utilizes MoU to improve the public safety of medical products. For example, there is MoU between US FDA and American Pharmacists Association (APhA). This MoU enables both parties to exchange capital information about medication error prevention, education, research, and training program for improving medical product safety (FDA, 2021).

A Mutual Recognition Agreement (MRA) may allow regulatory bodies to rely on each other information for drug or pharmaceutical product inspection. It may eliminate duplication of regulatory inspection which may improve inspection efficiency and permit resources reallocation for higher-risk manufacturing plants in other parts of the world (FDA, 2022). The US FDA implements MRA which may minimize the recertification process and replication testing which may support faster marketing approval decisions. The US FDA has some MRAs in place with the UK and the EU. These MRAs have specifically collaborated with the agency which regulates products that are covered by the US FDA. For example, two regulatory bodies in the UK which have MRA with FDA are the Veterinary Medicines Directorate and the UK MHRA.

The UK MHRA, like the US FDA, uses MRA to facilitate regulation. The MRA often includes not only pharmaceutical items, but also other commodities and products traded between the two nations. MRAs have been signed by the UK MHRA with the United States, Australia, Japan, and New Zealand, among others. This MRA may benefit the pharmaceutical industry by reducing the number of inspections performed at their facility and eliminating the need for goods to be re-tested upon import.

As a result, it is probable that the MHRA and FDA have comparable processes for implementing and utilizing MRA and MOU to improve their regulatory efficacy. By enforcing those agreements, they may be able to optimize actions and resources for analyzing, assessing, and inspecting certain files that are already being done by other parties or organizations.

## CONCLUSION

It is worth noting that government regulatory organizations, notably those for medicines, have their own set of rules and product scope. The guideline might be self-made or based on an agreement reached with other countries. Some product types are controlled by both the United Kingdom Medicines and Healthcare products Regulatory Agency (UK MHRA) and the United States Food and Drug Administration (US FDA). The particular method and standards for product authorization are defined by the UK MHRA and the US FDA. As a result, pharmaceutical manufacturers who intend to operate in related nations must examine and apply the regulatory body requirements that are in place.

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