International Journal of Pharmaceuticals and Health care Research (IJPHR)

IJPHR |Vol.12 | Issue 4 | Oct - Dec -2024

www.ijphr.com

ISSN: 2306-6091

DOI : https://doi.org/10.61096/ijphr.v12.iss4.2024.317-328

Review

Procedure And Regulations For Drug Registration In UK

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Published on: 12 Nov 2024

Published by:
DrSriram Publications

Abstract

MHRA (Medicines And Health Products Regulatory Agency) is the regulatory authority body for pharmaceuticals approval in the UK union. MHRA is formed by the merging of two separate agencies in 2003 i.e., Medicines Control Agency and Medical Device Agency. This agency works to maintain safety, quality and efficacy of the drug product before it enters into the country. The main aim of this work is to know about the practice and the regulatory requirements for the registration of a drug in the UK as per the regulations of MHRA. They are responsible for ensuring that the medicines and medical devices are acceptably safe and don't cause any harm to the patients. MHRA provides a license which is a marketing authorization to the manufacturer, required before a drug is being used by the patients of that country. Good Manufacturing Practice (GMP) is the minimum requirement that a manufacturer should possess during the period of production of the drug product. New drugs are being invented and also being distributed as per the needs of the patients. It is known that no drug product is completely safe or is 100% safe for use, but MHRA tries to minimize as many problems regarding the drug so that patients will be provided with the best drug with minimal risk.

Keywords: MHRA, United Kingdom, Product license, Ect

INTRODUCTION

Drug Regulation

The process of testing, developing and marketing of medicines has to regulated to protect the interests of the public. Major regulatory bodies include the Food & Drug Administration (FDA) in the US and the European Medicines Agency (EMA) in Europe. These bodies have various functions.

Licensing new medicines. New drugs are given a 'market authorisation' based on the evidence of quality, safety and efficacy presented by the manufacturer. The regulator will not only approve the drug but will also take great care to ensure that the accompanying information reflects the evidence that has been presented. This

document is known as the Summary of Product Characteristics (SPC) or 'label' provides detailed information about indications, dosage, adverse effects, warnings, monitoring etc.
Drug regulatory authorities often have other important functions including:

- Pharmacovigilance .
- Regulating clinical trials.
- Regulating herbal and homeopathic medicines.
- Inspecting and maintaining standards of drug development and manufacture.

Dossier

Dossier is a collection of papers giving detailed information about a particular person or subject. (or) a bundle of papers in reference to some matter or relating to a person[1]. (or) Dossier is a file document submitted to the Regulatory Authorities which contains detailed information about the drug product. In United Kingdom all drug products are classified into 3 categories based on their safety profile. Prescription only medicines (POM), Supervision of Pharmacist (P) and General Sale List (GSL). New medicines are usually authorized for use as Prescription Only Medicines (POM). After some years use, if adverse reactions to the medicine are few and minor, it is possible that the medicine may be safely used without a doctor's supervision. If there is sufficient evidence of safety, a medicine may be reclassified for sale or supply under the supervision of a Pharmacist (P). Pharmacy medicines which have been safely used for several years may be suitable for General Sale and may be reclassified as GSL[2]. The Medicines and Healthcare products Regulatory Agency (MHRA) is the regulatory agency in United Kingdom. MHRA is a government body which was set up in 2003 to bring together the functions of the Medicines Control Agency (MCA) and the Medical Devices Agency (MDA)[3]. These include the regulation of medicines and medical devices and equipment used in Healthcare and the investigation of harmful incidents.

A license, also referred to as a Marketing Authorization (MA), from the MHRA is required before any medicine can be used to treat people in the UK. Licenses for medicines are granted only when a product meets high standards of quality, safety and works for the purpose intended (efficacy). There are four types of procedures that applicants can take to obtain a Marketing Authorisation. To get a Marketing Authorisation in UK the applicant may choose any one of the four procedures those are Centralised Procedure (CP), National Procedure (NP), Decentralised Procedure (DCP) and Mutual Recognition Procedure (MRP)[4]. In these procedures the Centralized Procedure is mandatory for certain types of medicines and optional for others. The Centralised Procedure is administered by the European Medicines Agency (EMA) in London. It consists of a single application which, when approved, grants marketing authorisation for all markets within the European Union consisting of 28 countries and 3 EEA countries. CP is mandatory for Biotechnological Products and New Active substances for which the therapeutic indication is the treatment of AIDS, Cancer, Diabetes, Neurodegenerative disorder and Orphan products. In cases where national authorisations are requested for the same medicinal product in more than one Member State and the marketing authorisation holder has received a marketing authorisation in a Member State, the applicant/marketing authorization holder shall submit an application in the Member States concerned using the procedure of mutual recognition.

Drug Registration

It has been defined as: "a system that subjects all pharmaceutical products (under the scope of the NRA) to pre-marketing evaluation, marketing authorization (registration), and post-marketing review to ensure that they conform to required standards of quality, safety and efficacy established by NRA" . Registration of a new product is the first step of launching drug to the market of the Russian Federation. The registration is a state procedure of drug quality, efficiency and safety evaluation to obtain an approval for medical use of a drug in the Russian Federation. Registration of a new drug - the first step in the process of withdrawal of the pharmaceutical market of the Russian Federation. This procedure is essentially a state examination quality, efficiency and safety of the drug, which is held for the subsequent issuance of the permit on its medical use. In 2010, the drug registration procedure was essentially modified due to the adoption of new Federal Law No. 61-ФЗ "On circulation of medicines" of April 12, 2010 which became effective on September 01, 2010. To date, 4 modifications of the law have been adopted: No. 192-ФЗ of July 27, 2010, No. 271-ФЗ of October 11, 2010, No. 313-ФЗ of November 29, 2010, No. 409-ФЗ of December 06, 2011. Law of Russian Federation on December 22, 2014 N 429-FZ on "Amendments to the Federal Law" "On Circulation of Medicines ". Some of the introduced amendments will enter into force on 1 July 2015, another part - on 1 January 2016 and the last - more than a year, that is from January 1, 2017.

The procedure of drug registration

Stages of drug registration

Foreign and Russian drugs undergo identical registration procedure.
The registration procedure consists of 4 sequential stages:

1. Creation of a Registration dossier including documents necessary for clinical study initiation, and submission of the Registration dossier to the Ministry of Health of the Russian Federation.
2. Obtaining a permission for the conduct of a clinical study in the Russian Federation.
3. Drug quality evaluation and evaluation of the expected benefit to possible risk ratio which is done after the clinical study of a drug:
   The third stage may be divided into 2 sub-stages for convenience:
   1. Drug quality control at the FSBI SCEMP's laboratory and approval of a Normative document (specification and analytical procedures;
   2. Evaluation of the expected benefit to possible risk ratio and approval of Instruction for medical use of a drug.
4. Decision by the Ministry of Health of the Russian Federation on registration of the pharmaceutical product, it's entering in the State Register of pharmaceutical products and marketing authorization issuance.

Registration time-frames

According to Law No.61-Federal Law "On circulation of medicines", the period of the registration procedure is 210 working days. This period does not include the time required for conduction of a clinical study.

Stages of active pharmaceutical ingredient (API) registration, time-frames and costs.

The active pharmaceutical ingredients (API) can be approved for use (registered) in the territory of the Russian Federation in the following two ways:

1. As part of registration of a finished pharmaceutical product for which this API will be used. If the manufacturer intends to supply the API to a specific plant only, then information is provided and API quality evaluation is performed as part of the finished pharmaceutical product registration procedure. In this case, the API may only be used for the pharmaceutical product so evaluated.
2. Registration of an active pharmaceutical ingredients (API) not used in drug manufacturing. If the manufacturer has no decision to which plants he will supply his product and is going to expand the scope of his market, he is entitled to apply for registration of a API not used in drug manufacturing.

The API will be included in the State Register of registered medicinal products under a separate number.
Stages of registration of an active pharmaceutical ingredients (API) not used in drug manufacturing
Registration of a active pharmaceutical ingredient (API) consists of 2 stages:

1. API evaluation (quality control and approval of a Normative document (specification and analytical procedures));
2. Entering an API in the State Register of medicinal products.

The period of registration of a active pharmaceutical ingredients (API) not used in drug manufacturing: 5-7 months.

Drug Registration and Approval process in UK

The medicines and healthcare products regulatory agency (MHRA) regulate medicines, medical devices and other medical products for their approval in the United Kingdom. The agency protects and improves public health and supports all the innovations through scienti□c research and development programs.
The agency has three centers:

- The Clinical Practice Research Datalink (CPRD), a data research service which aims to improve public health with the help of NHS clinical data.
- The National Institute for Biological Standards and Control (NIBSC) which is a worldwide pioneer in maintaining the standards and Control of biological products.
- The Medicines and Healthcare Products Regulatory Agency (MHRA) which is the UK administrative body for medicines, medical devices and blood transfusion and furthermore in charge of guaranteeing the wellbeing, quality and viability of pharmaceuticals.

Not all the drugs can be considered as safe for use. In some cases, the drug can be effective as well as in some cases it may even lead to serious complications, resulting in death. The response of the people for medicines is different. Sometimes the medicines may cause severe side effects. The side effects are inuenced based upon the following-prescribed doses, treatment conditions, age and sex of the patient taking treatment. Medicines that are to be marketed will have to take a license from the regulatory authority based on the summary of the study that has been conducted on thousands of the people. When the study is done on thousands of people, some of the side effects are identified. Based on the safety of the drug the permission for the marketing of the drug will be issued. The medicines and healthcare products regulatory agency (MHRA) regulate medicines, medical devices and other medical products for their approval in the United Kingdom. The agency protects and improves public

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MHRA Process

The Process Licensing Office sits within the Inspectorate and Process Licensing Group of the Inspection, Enforcement and Standards division. It typically deals with the manufacture, assembly and wholesale distribution of medicinal products under UK and EU legislation, these licences are often called process licences and include:

- licences for the manufacture/importation of licensed medicinal products for human use, commonly abbreviated to MIA
- 'specials' licences for the manufacture/importation of unlicensed medicinal products for human use, commonly abbreviated to MS
- authorisations for the manufacture/importation of investigational medicinal products for human use, commonly abbreviated to MIA(IMP)
- authorisations for the manufacture/importation of licensed medicinal products for veterinary use (ManA)
- 'specials' licences for the manufacture of unlicensed medicinal products for veterinary use, (ManSA)
- manufacturer's licences for exempt advanced therapy medicinal products (MeAT)
- licences for the wholesale distribution of medicinal products for human use, commonly abbreviated to WDA (H) (including those covering unlicensed medicines obtained from another EEA member state)
- licences for the wholesale distribution/importation of medicinal products for veterinary use - WDA (V)
- blood establishment authorisations (BEA)
- non-orthodox practitioners (NOP)
- broker registrations
- active substance manufacturer, importer or distributor registrations
- certificates of Good Manufacturing Practice (GMP)
- certificates of Good Distribution Practice (GDP)

The MHRA Process Licensing Portal

The MHRA Process Licensing Portal is part of the government's Digital by Default agenda and is a web application which provides a secure environment and an easy to use platform which allows customers to submit new applications and variations to existing wholesale distribution authorisations electronically. The portal should be used for wholesale distribution authorisations [WDA(H)] and active substance manufacturers, importers and distributors – new applications, variation applications and annual compliance reports (active substance manufacturers, importers or distributors only).

MHRA is responsible for

- ensuring that medicines, medical devices and blood components for transfusion meet applicable standards of safety, quality and efficacy
- ensuring that the supply chain for medicines, medical devices and blood components is safe and secure
- promoting international standardisation and harmonisation to assure the effectiveness and safety of biological medicines
- helping to educate the public and healthcare professionals about the risks and benefits of medicines, medical devices and blood components, leading to safer and more effective use
- supporting innovation and research and development that’s beneficial to public health
- influencing UK, EU and international regulatory frameworks so that they’re risk-proportionate and effective at protecting public health.

- Scientific innovation
- Healthcare access
- Patient safety
- Dynamic organisation
- Collaborative partnerships
- Financial sustainability

These are underpinned by their priority to develop and improve patient and public involvement.
Types of MHRA licenses:
1. Pharmaceutical manufacturers
2. Import of medicines
3. Biological compounds and chemical compounds

How to license a medicine for sale in UK License for sale of a drug can be done by different procedures:
National procedure: This procedure is used when the drug has to be marketed only in the UK. A 5-digit company number and a PL number is to be obtained in the being of the procedure. The application process takes about 210 days. All the dossier and the informed consent checklist should be submitted, if the applicant is making an application for an informed consent marketing authorization.
Centralised procedure: It is required when the drug manufac-tured is to be marketed throughout Europe. All the new substance that is produced will take a single license when the substance has to be marketed in all European states as well as Norway, Iceland and Liechtenstein.
Decentralised procedures (DCP): It is needed if the drug has to be manufactured and marketed in the UK and other European

Types of MHRA licenses
1. Pharmaceutical manufacturers
2. Import of medicines
3. Biological compounds and chemical compounds How to license a medicine for sale in UKLicense for sale of a drug can be done by different procedures:

Types of application
- Full application- Article 8(3)
- Hybrid, generic or similar biological applications - Article 10
- Well established use application- Article 10a
- Fixed combination application- Article 10b
- Informed consent application- Article 10c

Abridged application procedure can be used in a certain application where pre-clinical and clinical studies are not needed. The types of application that can be used in this route are generic/biosimilars (Article 10), informed consent (Article 10c) and well-established use (Article 10 a) application. The legal basis for all types of application is set out in Directive 2001/83/EC and also in Regulation (EC) No726/2004.FeesPayment for the application should be done before submitting the document. The payment receipt should be attached along with application form. MHRA fee depends on the route of administration of the product that a manufacturer wishes to market. The proof of payment should be placed in the form of a PDF along with the application (eCTD).[11,12]
It should be one of the following:
- BACS or CHAPS electronic confirmation form.
- A photocopy of the cheque for the required sum with date and sign
- MHRA iRIS email account receipt (preferred for iRIS account holders)
- Email confirmation from MHRA finance department

Application process

Electronic common technical documentation method is used for the submission of application. In case if the applicant cannot submit by this method, non-electronic submission (NeeS) is also acceptable. MHRA checks whether the NeeS and e CTD are technically valid using the ExtendoEurs tool validation.

Active substance master files (ASMFs)

Active substance master file holders should submit their dossier to MHRA. Applicant must submit his active substance master file before the application being submitted or along with the submission of the application. If the active substance master file is not submitted then the application will not be valid unless the dossier of the

active substance is submitted.ASMF holder will have to register with the Common European Submission Platform (CESP) and then will have to submit their application through CESP.

Summary of product characteristics (SPC)

Using SPC (summary of product characteristic) template the manufacturer should submit a summary of the product characteristic to MHRA in the proper format using MS Word Document (36KB).

Ways to make a submission

Via Central European System Platform (CESP) manufacturer can submit the application. From January 2016, it is mandatory to submit electronic application forms (eAFs) for new marketing authorization, renewal and variation application submissions. This application submission is same for all the procedures (centralized, national or decentralized procedures). If submission of application is through portal way, then both portal form, as well as eAFs, should be submitted. If the application is submitted through CESP then, only eAFs submission is required.

Rejection of submissions

If the application that has been sent has any error or does not comply according to the need of MHRA, the application will be rejected. An email will be sent by the MHRA agency along with the correction that should be made in the application. Once the mail is received, the applicant will have to correct the mentioned errors and then resend the along with the correction. For the correction, no extra charges will be charged.

The European Union (EU) medicines regulatory system

The European Medicines Agency (or EMA) is the regulatory body in Europe that ensures that medicines are safe and that they work as expected. Located in London, the Agency is responsible for both human and veterinary medicines and has an important role in protecting public health in the EU. Working together with the national authorities of the 28 EU Member States as well as Iceland, Norway and Lichtenstein, the Agency is a key part of the European regulatory system for medicines. This collaborative model is the basis of the Agency's success as it gives the Agency access to a pool of experts (including regulators, academics, patients and healthcare professionals) from across the EU, giving it access to the best available scientific expertise.

Good Clinical Practice (GCP)

Good Clinical Practice (GCP) is an international ethical and scientific quality standard for the design, conduct, performance, monitoring, auditing, recording, analyses and reporting of clinical trials. GCP provides assurance that the data and reported results are credible and accurate, and that the rights, integrity and confidentiality of trial subjects are respected and protected.[10] It was finalised in 1996 and became effective in 1997, but was not enforced by law at that time. The Medicines for Human Use (Clinical Trials) Regulations 2004 and the European Union (EU) Directive on Good Clinical Practice changed the world perspective , and compliance with GCP is now a legal obligation in the UK/Europe for all trials involving the investigation of medicinal products.[14] It is very important to understand the background of the formation of the ICH-GCP guidelines as this, in itself, explains the reasons and the need for doing so ((Table 1)). The concept of the 'good physician'dates back to the ancient world and it is evidenced by the Hippocratic Oath (460 BC). In the United States, the first landmark in the regulation of drugs was the Food and Drugs Act of 1906.

Good manufacturing practice (GMP)

Good manufacturing practice (GMP) is the minimum standard that a medicines manufacturer must meet in their production processes. Products must:

- be of consistent high quality
- be appropriate to their intended use
- meet the requirements of the marketing authorisation (MA) or product specification

Good distribution practice (GDP) requires that medicines are obtained from the licensed supply chain and are consistently stored, transported and handled under suitable conditions, as required by the MA or product specification. Organisations that may have to comply with good manufacturing practice (GMP) and/or good distribution practice (GDP) include:

- manufacturer licence holders
- wholesale dealer licence holders
- blood establishment authorisation holders
- non-UK sites employed by UK MA holders

The inspection

The inspection team may ask for additional documentation and samples for testing during the inspection. They may also change the focus of the inspection if they suspect serious non-compliance. At the closing meeting the inspector will provide feedback and discuss any deficiencies with you and agree timelines for corrective actions.

Critical deficiency

A deficiency which has produced or significantly risks producing a product which is harmful to humans or veterinary patients or which could result in a harmful residue in a food-producing animal. Any departure from good distribution practice that results in a significant risk to patients. This includes an activity which increases the risk of counterfeit medicines reaching patients.

Major deficiency

A non-critical deficiency which:

- has or may produce a product that doesn't comply with its marketing authorisation
- indicates a major deviation from GMP or GDP or from the terms of the manufacturer licence or wholesale licence
- indicates a failure to carry out satisfactory batch release procedures or (within EU) a failure of the Qualified Person or Responsible Person to fulfil their legal duties
- a combination of several 'other' deficiencies which on their own may not be major but together may represent a major deficiency and should be explained and reported as such

Other

A deficiency which cannot be classified as either critical or major or there is not enough information to classify it as critical or major but which indicates a departure from good manufacturing and distribution practice.

Actions after the inspection

After the inspection closing meeting, you will receive a post inspection letter confirming any deficiencies found. You must respond to the inspector by email to confirm the proposed corrective actions and dates for when these actions will be completed. The inspector will review your response. If they accept it, you will receive a GMP or GDP certificate with your inspection report. An unacceptable response may lead to compliance escalation if further requests for information are unsatisfactory. If you're being inspected for GMP you should complete an interim assessment if there are changes to your site following your first inspection.

Guidance on responding to a post-inspection letter

The daily rate inspection fee includes preparation for, reporting andclose-out of the inspection. Inspections with critical findings or other significant non-compliance requiring referral to the GMDP Compliance Management Team and/or Inspection Action Group may require the inspector(s) to spend additional time beyond that covered by the daily rate overseeing the adequacy of the company's Corrective and Preventative Actions (CAPA) and the company's return to compliance. For such inspections, an office-based inspection fee may be charged for this additional time spent by the inspector(s) on such activities (for example, reviewing CAPA plans, impact assessments and periodic CAPA status updates).

Compliance escalation process

If your compliance is found to be poor but has not hit the threshold for regulatory action you may go through the compliance escalation process. The aim of this process is to support companies to achieve compliance before regulatory action becomes necessary. Once the process has been completed you will be returned to the routine risk-based inspection programme. However you could still be referred for regulatory action if you do not make the necessary improvements. The process may also be used if the Inspection Action Group has closed their case referral but the company to be monitored until remedial action plans have been completed. The process may include:

- making recommendations on close monitoring of compliance improvement work through inspection
- meetings and correspondence with company senior management clearly outlining the consequences of continued non-compliance

Good distribution practice (GDP)

Good Distribution Practices (GDP) is a quality system for warehouse and distribution centres dedicated for medicines. Internationally accepted pharmaceutical GDP regulations stipulate that distributors of pharmaceutical products must align their operations with the standard. Good distribution practice (GDP) describes

the minimum standards that a wholesale distributor must meet to ensure that the quality and integrity of medicines is maintained throughout the supply chain.
Compliance with GDP ensures that:

- medicines in the supply chain are authorised in accordance with European Union (EU) legislation;
- medicines are stored in the right conditions at all times, including during transportation;
- contamination by or of other products is avoided;
- an adequate turnover of stored medicines takes place;
- the right products reach the right addressee within a satisfactory time period.

The distributor should also put in place a tracing system to enable finding faulty products and an effective recall procedure. GDP also applies to the sourcing, storage and transportation of active pharmaceutical ingredients and other ingredients used in the production of the medicines.

Good Manufacturing Practice (GMP)

Good Pharmacovigilance Practice (GPvP) is the minimum standard for monitoring the safety of medicines on sale to the public in the UK. The MHRA inspects marketing authorisation holders (MAH) to determine whether they comply with pharmacovigilance obligations established within the UK. The MHRA inspects marketing authorisation holders (MAH) to determine whether they comply with pharmacovigilance obligations established within the UK. We have been conducting statutory GPvP inspections since 2003, and any UK MAH or marketing authorisation applicant (for any authorisation procedure) can be subject to GPvP inspection by MHRA, which may also include any of their partners or service providers.

Types of inspection

Inspections are typically scheduled by pharmacovigilance system, product or post-authorisation safety study, rather than by MAH. A pharmacovigilance system is defined as the system used by an organisation to fulfil its legal tasks and responsibilities in relation to pharmacovigilance and designed to monitor the safety of authorised medicinal products and detect any change to their risk-benefit balance. If a group of associated MAHs share the same pharmacovigilance system, all MAHs may be included within the scope of a single inspection of that pharmacovigilance system. Conversely, if an MAH operates more than one pharmacovigilance system, we usually review these through separate inspections. The MAH is usually notified of these inspections in advance. For inspections that cover products authorised in respect of Northern Ireland, our GPvP inspectorate shares the list of planned and conducted UK national inspections with the EMA and this is made available to all Eu Member States. If an inspection results in a critical finding it is likely the MAH will be subject to a triggered re-inspection within 12 to 18 months, with a focus on the actions that were agreed following the last inspection.

Triggered inspections

MHRA may perform a triggered inspection of an MAH in response to receiving specific risk information. For example, if we're informed about possible GPvP breaches by:

- a whistleblower
- other MHRA departments
- another regulatory authority

We may send little or no notification of these inspections in advance.

Pre-authorisation inspections

The majority of MHRA GPvP inspections are performed in the post-authorisation phase of the product life cycle. However, there are scenarios where pre-authorisation GPvP inspections of applicants for marketing authorisations are warranted and the objective of these inspections is to assess whether the applicant has the ability to comply with post-authorisation pharmacovigilance obligations.

Service Provider inspections

Increasingly, MAHs are outsourcing all or some of their pharmacovigilance activities to contract service providers; such activities conducted by these organisations on behalf of MAHs are subject to supervision by MHRA, including by means of inspection. Following a pilot programme of stand-alone service provider inspections, we concluded that a routine programme of inspections of pharmacovigilance service providers is not currently viable for the MHRA GPvP inspectorate. We continue to assess the activities performed by service providers in the context of MAH inspections. We may conduct stand-alone inspections of these organisations where it is deemed necessary to evaluate the overall system and procedures implemented by a service provider based on risk information available to the MHRA. Contracts with pharmacovigilance service providers should include provisions that cover the availability of data, documentation and appropriate support to the MAH and inspectors during a GPvP inspection.

Working with other regulators

MHRA GPvP inspection reports that cover products authorised in respect of Northern Ireland are shared with the EMA and EU/European Economic Area (EEA) Member States. Similarly, MHRA GPvP inspectors have access to inspection reports from other EEA member states. This information is taken account of when planning our inspections. It's important to note that a pharmacovigilance inspection by us at a site in the UK does not preclude other EU/EEA Member States from performing pharmacovigilance inspections at sites in their own country or in third countries (to fulfil national statutory obligations). Other EU/EEA competent authorities can contact the MHRA if they wish a site to be inspected in the UK. Looking further afield, Agency level agreements are in place to enable discussion of topics of mutual interest with several non-EU authorities and we have conducted GPvP inspections in non-EU countries such as Japan, USA and India.

Preparing for a GPvP inspection

Inspection notification

The majority of GPvP inspections are announced and are typically scheduled on a quarterly basis. As part of the inspection notification, the pharmacovigilance system master file (PSMF) will be requested. You must acknowledge you have received the notification and provide details of the relevant contact person for future correspondence about the inspection.

Pre-inspection documents

Prior to the inspection the lead inspector will contact the MAH and QPPV and provide the draft plan as well as any specific requirements of the team. In addition to the PSMF, inspectors may require supplementary information to confirm the scope of the inspection and to be well prepared. The lead inspector will explain how our document request system works.

Inspection location

To achieve the objectives for the inspection, inspectors will aim to be flexible with the plan and to accommodate changes, if possible. It is always preferable to conduct face to face interviews, however the inspection team can accommodate interviews by telephone/videoconference if interviewees are unable to attend the site, provided facilities are adequate to support this. If the MAH does not have a UK site and is using a vendor site or hiring office space for the inspection, consideration should be taken to ensure access to WIFI and teleconference facilities (if required) throughout the inspection, as well as prompt access to printing and copying facilities, and access to all electronic documentation and systems including the live safety database. The inspection will typically require the use of at least one main inspection room and the company may wish to have a 'back-room' for the preparation of document requests.

Remote inspections

Routine and triggered inspections may be conducted by inspectors remotely. These inspections are conducted through review of requested documents including evidence to support pharmacovigilance activities and submissions. The document review is supplemented with telephone interviews with relevant subject matter experts and written responses to specific queries. Logistical aspects of the inspection, including timings and availability of specific subject matter experts and the QPPV for telephone/videoconference interview, are arranged with the inspected organisation prior to the inspection. An onsite inspection may be triggered following the remote inspection, should any significant non-compliance or concerns that require further investigation be identified.

Unannounced inspections

On rare occasions, inspections may be conducted unannounced. Under UK law, an inspector acting on behalf of the MHRA (as licensing authority) has the right, at any reasonable time, to enter premises (not limited to those of the MAH) to determine if there has been a contravention of the regulations laid out in SI 2012 No 1916 as amended (per Regulation 325) and the right to inspect information and documents relating the requirements for pharmacovigilance laid out in Part 11 of SI 2012 No 1916 (as per Regulation 327). In short, although rarely done, the MHRA GPvP inspectorate can arrive at, and enter UK sites relating to the conduct of pharmacovigilance activities without notifying the MAH first. In this instance, on arrival at site the lead inspector will identify the most appropriate person on site as a point of contact and will explain the purpose and logistics of the inspection.[15]

The inspection

During an inspection the inspection team may:

- conduct site visits
- interview relevant personnel
- review documents
- carry out computer system reviews including searching pharmacovigilance databases

The inspection team will ask for additional documentation during the inspection. They may also change the focus of the inspection if they suspect serious non-compliance.

The team and inspection duration

Inspection teams are comprised of between one to four inspectors, spending between two and five days on site. This can vary based on the type of products marketed by the company, the complexity of the pharmacovigilance system and the type of inspection (for example routine or, triggered). Occasionally observers may also be present at our inspections. This may include representatives from the MHRA's Vigilance and Risk Management of Medicines (VRMM) division and Enforcement Groups or other regulatory authority inspectorates.

Inspection conduct

Inspectors normally interview operational personnel that are involved in pharmacovigilance activities or activities associated with pharmacovigilance including regulatory affairs, and management of post-authorisation safety studies. If considered necessary, for example if serious issues are identified relating to a business area, it might be necessary to interview a senior executive and senior executive(s) might be requested to attend the closing meeting.

DISCUSSIONS

The regulation of therapeutic goods, defined as drugs and therapeutic devices, varies by jurisdiction. In some countries, such as the United States, they are regulated at the national level by a single agency. In other jurisdictions they are regulated at the state level, or at both state and national levels by various bodies, as in Australia.

The role of therapeutic goods regulation is designed mainly to protect the health and safety of the population. Regulation is aimed at ensuring the safety, quality, and efficacy of the therapeutic goods which are covered under the scope of the regulation. In most jurisdictions, therapeutic goods must be registered before they are allowed to be sold. There is usually some degree of restriction on the availability of certain therapeutic goods, depending on their risk to consumers.

Regulatory authority

The Medicines and Healthcare products Regulatory Agency (MHRA) is the regulatory agency in United Kingdom. MHRA is a government body which was set up in 2003 to bring together the functions of the Medicines Control Agency (MCA) and the Medical Devices Agency (MDA). These include the regulation of medicines and medical devices and equipment used in Healthcare and the investigation of harmful incidents. The MHRA also looks after blood and blood products, working with UK blood services, healthcare providers, and other relevant organisations to improve blood quality and safety. Requirements for registration of medicinal products in the United Kingdom: A license, also referred to as a Marketing Authorization (MA), from the MHRA is required before any medicine can be used to treat people in the UK. Licenses for medicines are granted only when a product meets high standards of quality, safety and works for the purpose intended (efficacy). The regulatory system also imposes rigorous standards on medicines manufacturers and wholesale dealers who trade in them. The licensing system guarantees accountability for all those involved and ensures that processes, supplies, and quality can be thoroughly monitored and swift corrective action taken where necessary. The authorization process for devices differs from that applied to medicines. However, once marketed, safety and performance of medicines and medical devices are monitored and enforced in similar ways. To begin the process, companies and/or researchers must apply to the MHRA for permission to test drugs through clinical trials, if these trials are to be conducted in the UK. In order to receive permission to run a trial, they must first satisfy the MHRA that they have met strict safety criteria. All the test results from these trials on how well the medicine works and its side effects, plus details of what the medicine contains, how it works in the body, and who it is meant to treat, are then sent to the MHRA for detailed assessment. The assessment team is made up of experts from different relevant specialties, each of whom has undergone additional training in medicines assessment. The length of the assessment process depends on the type of medicine as well as the quality of the initial information supplied by the manufacturer, how much further detail is required, and how soon queries can be resolved. In the past, all this information used to be supplied in paper format; now it is supplied electronically, to minimize procedural delays. MHRA also has to comply with strict timeframes and performance targets for the licensing of medicines. Once the MHRA is satisfied that the medicine works as it should, and that it is acceptably safe, it is given a marketing authorization or product license. The pharmaceutical company and any wholesalers must also be able to satisfy the MHRA that the manufacture, distribution, and supply of the medicine meet the required safety and quality standards. Marketing Authorization procedures: There are four types of procedures that applicants can take to obtain a Marketing Authorisation. To

get a marketing authorisation in United Kingdom the applicant may choose any one of the four procedures those are:

1. National Procedure.
2. Centralised Procedure.
3. Decentralized Procedure.
4. Mutual Recognition Procedure.

CONCLUSION

Any medicinal agent to be marketed in the United Kingdom has to follow the guidelines and egulations framed by MHRA, a regulatory authority which approves the drug products. The objective of this review article is to highlight information regarding the requirements, the different types of submissions for the registration of a medicinal product in a market in the UK. It also includes all the details about the fee for the application and the time period for the approval of the application after the submission of the application. By knowing the requirements of the MHRA guidelines and regulations, it is easy for a product to get into the UK market.

Any medicinal agent to be marketed in the United Kingdom has to follow the guidelines and regulations framed by MHRA, a regulatory authority which approves the drug products. The objective of this review article is to highlight information regarding the requirements, the different types of submissions for the registration of a medicinal product in a market in the UK. It also includes all the details about the fee for the application and the time period for the approval of the application after the submission of the application. By knowing the requirements of the MHRA guidelines and regulations, it is easy for a product to get into the UK market. United Kingdom has a major marketing value for pharmaceuticals it is one of the top ten major pharmaceutical markets. Present study is explained in brief about the Marketing Authorisation procedures and Dossier requirements i.e, Quality requirements, Bioequivalence and Labelling requirements for a prescription drugs (generics). So by knowing the Regulatory landscape of this Region it is helpful in getting a marketing authorization from MHRA.

ACKNOWLEDGEMENT

The Authors are thankful to Sura Pharma Labs, Dilshukhnagar, Hyderabad for providing the necessary facilities for the research work.

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