



# Medicines & Healthcare products Regulatory Agency



12 Nov-19



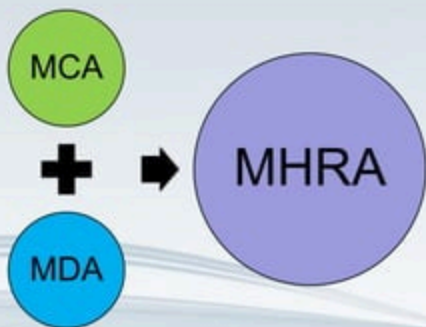
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# Introduction

The Medicines and Healthcare products Regulatory Agency (MHRA) is a government body which of the Department of Health of United Kingdom was set up in 2003 to bring together the functions of the Medicines Control Agency (MCA) and the Medical Devices Agency (MDA).



# History

❖ In 1999, the Medicines Control Agency (MCA) took over control of the General Practice Research Database (GPRD) from Office for National Statistics.



❖ Medicines Control Agency (MCA) and the Medical Devices Agency (MDA) merged in 2003 to form MHRA.

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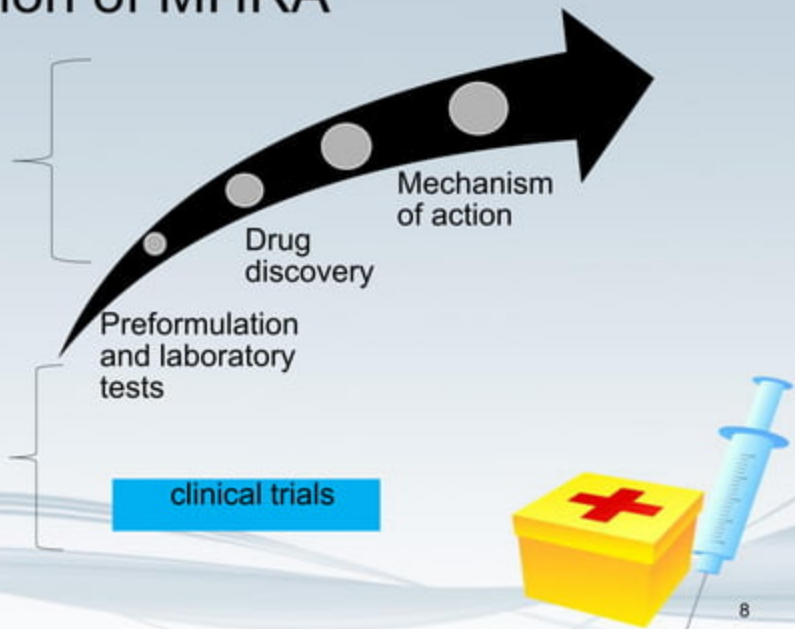
- ❖ In April 2012, the GPRD was expanded and re-launched as the Clinical Practice Research Data-link (CPRD).
  
- ❖ In April 2013, MHRA merged with the National Institute for Biological Standards and Control (NIBSC) and was rebranded, with MHRA identity being used for the parent organization and one of the centres within the group. At the same time CPRD was formally declared a separate centre of MHRA, too.



# Function of MHRA

The MHRA has no interest in these early stages of drug development.

MHRA comes in play when the company wants to start clinical trials in patients.



# MHRA functions

- ❖ Regulation of clinical trials
- ❖ Safety and efficacy monitoring
- ❖ Providing information to public and health professionals
- ❖ Licensing
  - ❖ Manufacturer and dealer licenses
  - ❖ Clinical trial licenses
  - ❖ Parallel import licenses
- ❖ Enforcement of law

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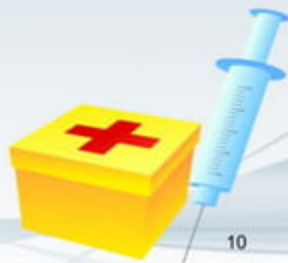
# Development new drugs

## 1. Discovery

- A fundamental first step to discovering new drugs is knowledge of the biology of a disease. This involves understanding how cell and biological processes work in health as well as what goes wrong in disease. This will reveal potential targets that a drug could act on.
- Studies in cells and animals are crucial first steps and should not be undervalued. However, many drugs that show promising results in cells in laboratories don't work in animals, and many drugs that show promising results in animals don't work in humans.
- Many thousands of new chemical compounds are created and tested to identify those that have potential. There is a very high drop out rate at this stage; fewer than 1 in 1,000 of all the compounds that are made ever progress to testing in humans.

## 2. Phase I

- The first step in testing a new drug is to determine the safety of single doses in a small number of healthy volunteers.





### 3. Phase II

If the treatment proves to be safe, studies begin to determine the effectiveness of the drug in people with the condition to be treated. The study may be:

- ❖ controlled - the drug is compared with the standard treatment or placebo (dummy treatment)
- ❖ double-blind - neither the investigators nor the participants know which treatment they are receiving
- ❖ randomized - participants will be randomly allocated to receive active treatment or placebo.

### 4. Phase III

- If a drug shows effectiveness, a larger study is conducted in hundreds of people.
- Phase III studies in relapsing remitting MS generally run for two years and compare the number of relapses in people taking the new drug with those taking the standard treatment or placebo.



## 5. Licensing

Data from all of these three phases is presented to the regulatory authorities (in the UK this is the MHRA - Medicines and Healthcare products Regulatory Agency or the EMA - European Medicines Agency). If the authorities are satisfied that the new medicine is effective, safe and meets manufacturing quality standards, a marketing authorization or license is issued.

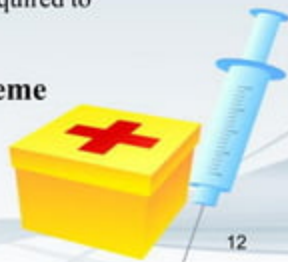
## 6. NHS appraisal

- ❑ Once a new medicine has been licensed, there may still be one final hurdle. Set up to help eliminate postcode lottery prescribing, NICE (National Institute for Health and Care Excellence) for England and Wales and SMC (Scottish Medicines Consortium) for Scotland appraise certain new medicines and will look at issues such as cost effectiveness of the new treatments.
- ❑ The NHS is legally obliged to fund medicines recommended by NICE or SMC. The reverse also holds true – if NICE or SMC do not approve a new medicine, then local health authorities are not required to provide funding for it.

## Post-marketing surveillance and Yellow Card Scheme

- ❖ Once the newly-licensed medicine is in general use, it will be carefully monitored for safety. All medicines have a patient information leaflet (PIL), which gives instructions on how the medicine should be used, and on its side effects.

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- ❖ In the UK, the Yellow Card Scheme is used by doctors and members of the public to report unwanted side effects of a medicine to the MHRA.

## New uses of a medicine

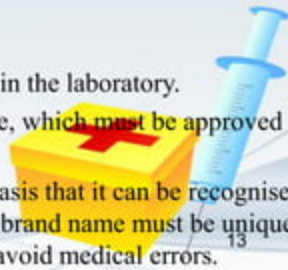
Clinical trials will continue after a medicine has been granted a license. These trials aim to:

- find new treatment uses
- compare the new medicine with other treatments
- determine effectiveness in a much wider range of patients
- assess long term benefits and safety

A license is granted for a specific use and in a particular group of people. However, once a medicine has been approved for one purpose, doctors are free to prescribe it for any other purpose that in their professional judgment is both safe and effective this is described as off-label use.

## Naming of drugs

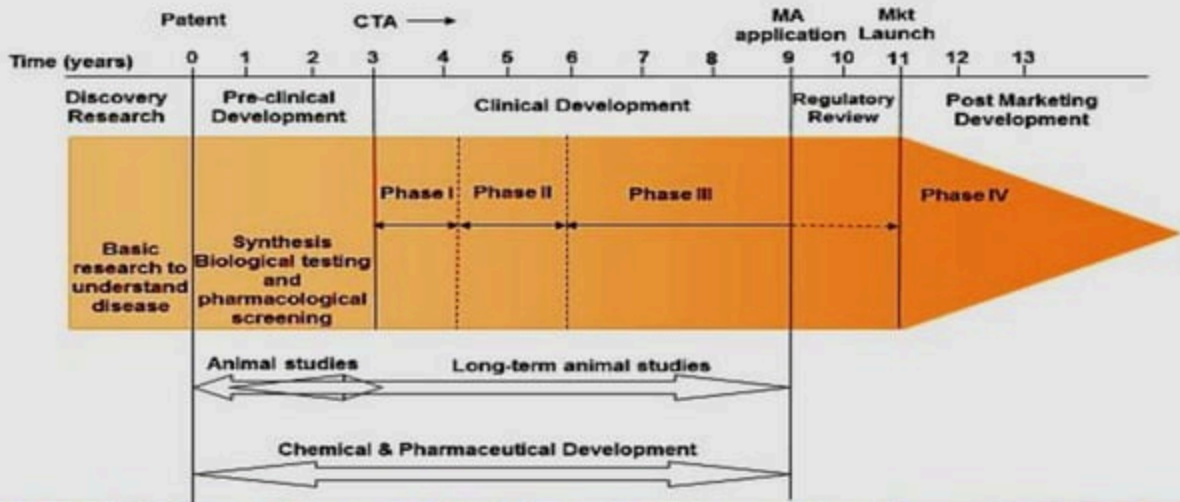
- ❑ Drug names usually start as a string of letters and numbers, a name used to identify it in the laboratory.
- ❑ As the drug advances through testing, it gets a generic name, or non-proprietary name, which must be approved by the World Health Organization.
- ❑ The brand name, or proprietary name, is chosen by the manufacturer, usually on the basis that it can be recognised, pronounced and remembered by health professionals and members of the public. The brand name must be unique to protect the trademark and not sound or look too much like any other drug name to avoid medical errors.



# Drug Development Process



**MHRA**  
Regulating Medicines and Medical Devices



# Process of Licensing

Application  
for clinical  
trials

Evaluation  
by MHRA

Does not  
satisfy

Satisfy

clinical trials

clinical trials  
results

Gives marketing  
authorization

Satisfy

Assessment  
of data by  
expert

No license

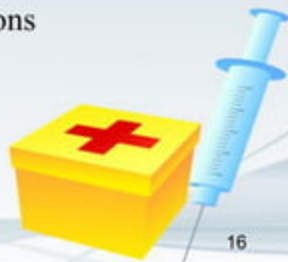
Does not  
satisfy



# The MHRA licenses / authorizes

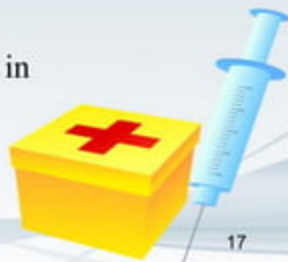
- ✓ Pharmaceutical manufacturers
- ✓ Medicine importers
- ✓ New biological or chemical compounds
- ✓ Different brands of existing medicines
- ✓ Generics (identical but cheaper versions of existing branded medicines)
- ✓ New forms of existing medicines, such as syrups, patches, or injections
- ✓ New uses for existing medicines, such as different patient groups or different conditions
- ✓ Reclassification of medicines from

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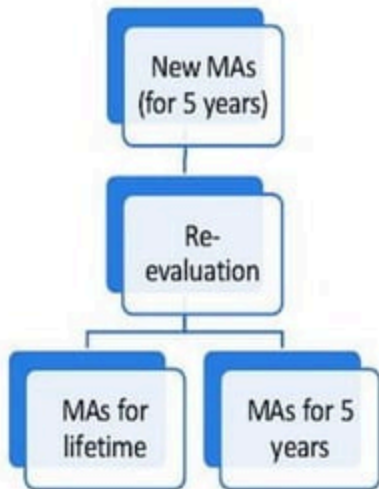


- ✓ prescription only to over the counter use, such as the cholesterol lowering medicine Simvastatin (Zocor Heart-Pro)
- ✓ Traditional herbal medicines sold over the counter that meet required safety and quality standards
- ✓ Designated authorities (Notified Bodies) that approve the quality marking system (CE marking) for medical devices /equipment
- ✓ Clinical trials of both medicines and devices, from toothpaste to gene therapy
- ✓ Blood banks that meet required safety and quality standards
- ✓ Applications on humanitarian grounds to use certain medical devices in the UK not carrying a CE marking



# Renewal of license

- New Marketing authorizations (MAs) are valid for five years and then may be renewed on the basis of a re-evaluation of the risk- benefit balance.
- Once renewed, the marketing authorization will be valid for an unlimited period.
- Applications for renewal should be submitted at least six months before expiry.





# Cancellation of license

- ❖ If MAs holder does not file an application for renewal within specified time, MAs expires automatically.
- ❖ If the MAs holder does not wish to renew the license, a letter should be sent indicating the cancellation to:
  - ✓ Administrative Support Team
  - ✓ Medicines and Healthcare products Regulatory Agency (MHRA).
- ❖ MHRA has authority to cancel license of product if it affects public health.

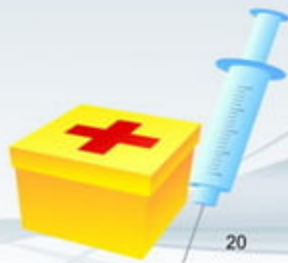


# Export drugs and medicines

Permission must need to export certain drugs and medicines.

These are:

- ✓ Controlled drugs
- ✓ Drugs that can be used for lethal injections
- ✓ Medicines
- ✓ Export certificates for medicines for animals



## Controlled drugs

- ❑ Check the list of common controlled drugs.
- ❑ If your drug is controlled, need a Home Office controlled drug license to export it. This is in addition to any domestic license you need to possess the drug in the UK.
- ❑ If drug is not on the list but you think it might have the properties of a controlled drug, check the relevant legislation to find out if it's controlled. The list of common controlled drugs has links to the relevant legislation.

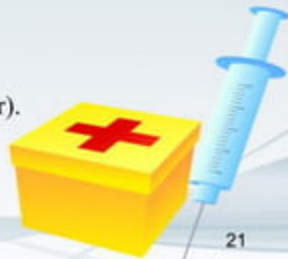
### Apply for an export license

- ❖ Need a Home Office controlled drug license to export controlled drugs anywhere in the world.

To apply:

- ✓ register for a Home Office controlled drugs license
- ✓ log in once has registered
- ❖ License will be valid for up to 2 months (or until your import permit expires, if sooner).

**Fees:** The export license costs £24.



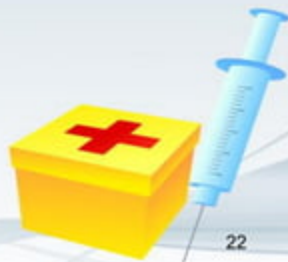
# Drugs that can be used for lethal injections

## Medicines

### ➤ Export certificates for medicines for humans

There are 5 types of certificate. Which one you need will depend on the requirements of the importing country. Talk to the importer who's receiving your goods to find out.

1. Certificate of a pharmaceutical product (licensed)
2. Certificate of a pharmaceutical product (unlicensed)
3. Certificate of manufacturing status
4. Certificate of licensing status
5. Certificate for the importation of a pharmaceutical constituent



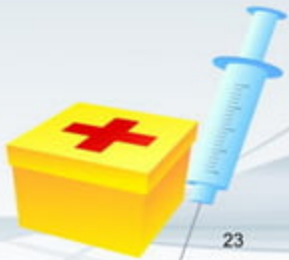
- ❑ If your application is successful, you'll get the original version of your certificate and 2 copies.
- ❑ You can get extra copies of certificates for £34 each.

➤ **Export certificates for medicines for animals**

There are 5 types of certificate. These are:

- a) Defra-1
- b) Defra-2
- c) Defra-3
- d) Defra-4
- e) Defra-SFA

- ❖ Anyone should get certificate or be told why it hasn't been issued within 10 days.
- ❖ The fee is £30 (plus £15 for each certified copy, if anyone need these).



## Import a human medicine

- Import a licensed medicine
- Import an unlicensed medicine
- Make an urgent import notification

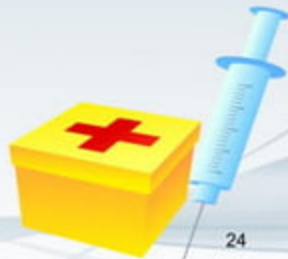
## Import a licensed medicine

- Wholesale
- Manufacturer
- Marketing authorization (MA)

## Import an unlicensed medicine

- Import an introduced product
- Import a special product

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## Make an urgent import notification

- ❖ In cases of clinical emergency (usually the treatment of life-threatening illness or where significant injury is likely) MHRA is able to process an import notification within one working day.
- ❖ Commercial or other non-clinical reasons aren't acceptable reasons for urgency.

## Fees

Fees are charged annually using a banding system based on the number of notifications anyone submit. Customers are provided with an estimate early in the financial year, followed by an invoice once all the information for the year is available.

A doctor may make the request to a licensed importer, or to a pharmacist who then places the order with the importer. If a doctor or pharmacist holds their own wholesaler or specials license, they can make the order themselves.

## Fees for safety and quality vetting of unlicensed imported medicines

Combination medicines and products, which have two different medicines within one pack, are considered a single notification. Separate packs of different products would require separate notifications.



thank you.

