

# Developing, registering and using medicines



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## 13.1 Introducing medicines

This chapter deals with three areas affecting the rights of health care users:

- Developing medicines – how new medicines are discovered and researched to prove that they are safe and do what they are designed to do.
- Registering medicines – the process of obtaining permission to sell medicines.
- Using medicines – the prescribing/dispensing by doctors and pharmacists, and the purchasing and consuming of medicines by the public.

Medicines are far more than just a commodity used in the delivery of health care services. Whether or not they are available to health care users (patients) when needed is often seen as a very sensitive indicator of the performance of the health care system. Users will often characterise their lack of satisfaction with the services they receive by stating that medicines they want are not available. Everyone has seen reports of users complaining: “All they have got for us is Panado”.

In addition, modern medicines have been responsible for at least part of the major advances seen in health care in the last century. Diseases that were previously fatal are now more easily treated.

Examples: Drugs that treat diseases

- Insulin to treat diabetes mellitus.
- Penicillin antibiotics for diseases caused by bacteria, such as pneumonia.

For these reasons medicines, also often referred to as ‘drugs’, cannot be regarded as normal articles of trade. They have properties that make them different from ordinary consumer goods. These properties mean that the supply and use of medicines need to be regulated and controlled by law. But in addition, because medicines are so essential to health and well-being, access to them has become one of the most burning human rights questions of the 21st century.

### How medicines are different from other commodities

Medicines differ from ordinary commodities in three crucial ways:

- They have a three-tiered demand structure between the person who needs them (the user), the person who prescribes them (the doctor) and often the person who pays for them (such as the medical aid scheme).
- Their technical quality is difficult to assess, except by trained pharmacists.
- Information about them can be unbalanced and subject to bias, particularly when they are marketed in competition with other medicines.

We can understand these differences by contrasting the purchase of a medicine and a shirt. While a shirt may be important to keep you warm, the decision to buy one is usually not made when you do not have a shirt. The decision to purchase a medicine is, however, often made when you are ill.

The decision to buy is therefore not a voluntary one. In fact, the decision may not always be taken by the user, but may rather be made by someone else, like a medical doctor. If you are insured or a member of a medical aid, that "third party" may also pay for the medicine. Although the user is the ultimate consumer of the medicine, the power of the consumer is usually limited.

While you may feel quite comfortable judging the quality of a shirt, you may not feel as comfortable judging the quality of a medicine. The "technical quality" of a medicine is very difficult for an untrained person to judge. For example, an ordinary user of a medicine will not be able to answer whether it dissolves properly, or whether the medicine releases the right quantity of the active ingredient.

The information available to both prescribers and consumers is often selective, unbalanced or incomplete. Market forces of supply and demand do not operate efficiently with medicines, particularly those that are protected by patents – this means that there is limited competition between suppliers of patented medicines.

For more on market forces and patents, see 14.2 on page 439.

## Positive and negative external effects of medicines

Perhaps most importantly it is necessary to understand how medicines have what are called "positive and negative externalities". *Externalities* refer to the external effects of the medicine (rather than the effects on the person being treated).

- Treating someone with an infectious disease such as tuberculosis (TB) not only benefits that person, but has the additional "positive" external value of reducing the spread of the infection to other people.
- If the person is not able to access the necessary treatment, the risk of spread of the disease will be increased (a "negative" external effect).
- If access to medicine is difficult, this may discourage users from seeking help from a health facility. Again, this may increase the spread of disease.

Thinking not only about the effect on the individual, but of the effect on the whole community is known as "a public health approach".

## 13.2 Developing medicines

People have used whatever came to hand to treat disease since the beginning of time. What makes the modern era different is that the making and supply of medicines has become a commercial operation.

### From natural to chemical materials

In the most recent times – especially from the early part of the 20th century – medicines have become increasingly based on synthetic chemicals, rather than herbal or plant-derived materials. While this process has resulted in more potent, site-specific and sometimes less toxic medicines with minimal side effects, it has not eliminated all the potential risks.

Very potent chemical compounds with major effects on the human body have also been developed. These can benefit people, as well as be risky if they are not used properly. The most famous example of this involved children born to women who had taken thalidomide, a medicine for morning sickness, who suffered major physical deformities. This was the spark that created a new wave of government intervention internationally in the mid-1960s.

### Discovering medicines

Medicines are discovered in a number of ways, including:

- Developing drugs to target specific diseases.
- Observing benefits and alternative usage by accident.
- Developing modern medicines from natural sources.

A new drug is a designed chemical aimed at a known biological target in the body. Knowledge of the properties of the target and how it is involved in the disease process allows a specific chemical to be designed that will exert an effect on the target.

Example: Enfuvirtide

Understanding how the Human Immunodeficiency Virus (HIV) fuses with the human CD4+ cell has allowed for the deliberate design of a fusion inhibitor molecule, called enfuvirtide. This stops HIV from duplicating itself inside the human cell, because it cannot enter the cell.

Many useful medicines have also been found entirely by accident to have therapeutic properties.

### Example: Penicillin

Penicillin, an antibiotic used in the treatment of bacterial infections, was discovered in 1928 when Alexander Fleming observed the effect of mould on bacterial growth.

In addition, medicines developed for one purpose have sometimes proved useful in treating other diseases. For example, many medicines used for epilepsy can also be used to manage chronic pain caused by nerve damage. Similarly, while the antiretroviral drug, nevirapine, was developed to treat AIDS, it later proved to have a powerful effect in preventing the transmission of HIV from a mother to her child.

### Building on natural sources

Many medicines were originally found as chemical substances in plants, but have been isolated and are now made in a factory.

#### Examples: Medicines originating in plants

- Aspirin is one of the most widely used medicines in the world, but originally it came from the bark of a willow tree.
- For many years quinine was the primary medicine used in the treatment of malaria. It was extracted from the bark of the cinchona tree, found in South America.

Plants are still being investigated or even used as a source for modern medicines.

#### Examples: New medicines from plants

- New anti-malarial medicines from a Chinese herb (*Artemisia annua*).
- Potentially useful appetite suppressants from a plant used by the San people (*Hoodia gordonii*).

For more on traditional medicines, see Chapter 7.

For more on health research, see Chapter 12.

## Phases of developing medicines

Whatever its initial process of discovery, the development of a modern medicine follows two critical phases:

- Pre-clinical development.
- Clinical development.

### Pre-clinical phase

In the pre-clinical phase, the safety of the new chemical is investigated. Safety testing is mainly done in animals, for example to test for unexpected effects in a healthy animal. These steps must generate sufficient data before the chemical can start to be tested in humans.

Testing each medicine for safety is essential because quite similar medicines can have very different effects. For example, the antiretroviral nevirapine is safe for use in pregnancy, but another ARV, efavirenz, has been shown to result in deformities in monkeys and can therefore not be used in pregnant women.

Early work on scaling up the synthesis of the active ingredient and studying how best to make this into an effective medicine are also done in this phase. This work is also called “formulation studies”.

### Clinical phase

For medicines:

- *Safety* means its tolerability and side effects.
- *Efficacy* refers to whether or not it works.

The clinical phase of development has four sub-phases:

- *Phase 1*: Evidence must be gathered on the *safety* of the new chemical in small numbers of healthy volunteers.
- *Phase 2*: The new chemical will then be tested in small numbers of volunteers to assess efficacy and dosing. These may be volunteers who:
  - have the disease of interest (treatment), or
  - are at risk of the disease of interest (preventative medicine).
- *Phase 3*: Only when Phase 2 evidence is available, will permission be granted to test the new chemical in larger numbers of subjects under well-controlled conditions. This final stage of experiments – called Phase 3 trials – will provide the necessary evidence to decide whether the new chemical is effective in its intended use.
- *Phase 4*: The process of development continues even after the medicine is made available on a commercial scale – in other words, after it has been registered as “approved for sale to the public”. Evidence is gathered in planned Phase 4 post-marketing surveillance trials and from the experience of users of the medicine. This is when there may be further discoveries as a result of observation about a medicine’s use. From this evidence:
  - Unexpected and rarer side effects may be uncovered.
  - The recommended dose of the medicine may also be changed.

## Costs, risks and rights in developing medicines

The cost of developing a modern medicine is high and the process includes a number of risks. There are risks to the study participants and also commercial risks for the funders of the research process.

How high these costs are and how high the risk of failure is, are controversial issues. Estimates of the cost of developing a new medicine vary, depending on the methodology used. Figures as high as US\$800 million are claimed by pharmaceutical companies, but consumer groups that monitor medicine development, such as the Consumer Project on Technology in the USA, say that the true cost may be a quarter or less of this figure.

Governments sometimes make quite large investments in the initial stages of development. However, the pharmaceutical industry usually bears the costs of the final stages of putting the medicine into a form that can be administered to users and getting the final authorisation to sell the medicine.

### Rights of research participants

There is a range of policies and laws that closely protect the rights of research participants, who are absolutely vital to the medicine development process. These are described in detail in Chapter 12. In South Africa, clinical trials can be conducted only after the Medicines Control Council (MCC) has approved them. The process of obtaining this permission is outlined in the Medicines Act (see below in 13.3) and its Regulations, and is also covered in Guidelines produced by the MCC.

Both the South African Medical Research Council and the Department of Health have produced extensive guidelines on the protection of the rights of human participants in clinical trials.

The National Health Act 61 of 2003 has also tightened control over the research ethics committees that oversee these activities at universities and other research bodies, including those in the private sector.

For more information on research structures, see 12.5 on pages 402–403.

### Key Point: Confidentiality

At all times, the confidentiality of information gathered during research must be assured – this is the rule for any health care process.

## 13.3 The role of the Medicines Control Council

As medicines are considered to be “meritorious goods”, the Government has a responsibility to intervene to ensure safe, affordable and appropriate access. The most important structure involved in this system of control in South Africa is the Medicines Control Council (MCC).

In the mid-1960s, the thalidomide tragedy made many governments realise that all medicines should first be fully tested before they could be sold to the public. South Africa’s Medicines and Related Substances Control Act 101 of 1965 (Medicines Act) was first passed in 1965, although it has been amended many times since then. Before 1965, medicines could be sold without the manufacturers having to prove that they were safe or that they actually worked as was claimed.

### Introducing the MCC

The Medicines Act created the MCC, a statutory body, with the express aim “to provide for the control of medicines”. The Act allows the Minister of Health to appoint an MCC made up of people with expertise in areas such as:

- *Pharmacology* – the study of the effects of drugs in human and animals.
- *Pharmaceutical chemistry* and *pharmaceutics* – the chemistry and science of making medicines into forms that can be administered.
- The *clinical management* of disease in humans (eg physicians) and animals (eg veterinarians).

Importantly, an amendment to the Act that eventually came into force in 2003 states that none of the MCC members may be employed in the pharmaceutical industry. Members who have ties with the industry in any way must disclose them.

The work of the MCC is supported by a secretariat of full-time staff. Although the Act has provided for this secretariat to exist outside of the public service, at present it is organised as a “cluster” of the National Department of Health (NDoH), known as the Medicines Regulatory Affairs (MRA) cluster. For an organogram illustrating the structure of the NDoH, see page 109.

The Medicines Act covers the supply and regulation of:

- Medicines for human and veterinary use.
- Biological products, such as vaccines and blood products.
- Medical devices, such as neonatal incubators, masks and pumps and instruments used in surgery.

## Registrar of Medicines

The chief director of the MRA cluster in the NDoH also serves as the Registrar of Medicines. The key task of the Registrar is to keep the Register of Medicines. This is the list of all medicines approved for sale in South Africa.

## Registering medicines

Anyone wishing to sell a medicine in South Africa must first register that medicine with the Medicines Control Council (MCC). In order to be registered medicines must demonstrate three key qualities before permission to sell is granted:

- Safety.
- Quality.
- Efficacy.

Unfortunately, the volume of work that must be done by the MCC far exceeds the capacity of its members (a maximum of 24, according to the Act). All of the Council members are part-time appointees.

## Expert committees

The Council appoints expert committees that are asked to consider parts of the applications made to the Council and to make recommendations. These include committees that study:

- Pre-clinical and clinical data.
- Pharmaceutical and analytical data.
- Clinical trials.
- Complementary medicines.

While one committee may study clinical data, another will make recommendations on whether or not the medicine can be made available only on prescription or whether health care users can buy it elsewhere – this is referred to as recommending the "scheduling status" for the medicine. This committee will also approve the trade name of the medicine that the company chooses.

## Key Points: Chemical and brand names

Medicines usually have two names:

- A chemical name, also referred to as a *non-proprietary name*.
- A trade name or brand name, also called the *proprietary name*.

For example, one of the companies that make nevirapine sells it as "Viramune". Nevirapine is the chemical name. Viramune is the trade or brand name.

## Pharmacovigilance

The MCC also has an expert committee that looks at data generated after the medicine has been approved for use – this is called pharmacovigilance data. Pharmacovigilance data are used to identify new side effects that become apparent only when large numbers of users use a medicine, and where necessary, to change the way in which that medicine is used.

## Ensuring safety

Safety data comes from two main sources:

- The pre-clinical studies conducted in animals, before the clinical development phase commences.
- Observation and reports on side effects encountered during the clinical phases, both in healthy volunteers and in health care users.

On the basis of this information, the MCC must make a decision on the balance between the risks associated with the medicine and its anticipated benefits.

Examples: Balance of risks and benefits

- A medicine that is intended to treat a very serious and life-threatening disease, such as cancer, may be acceptable even if it is associated with considerable risks. Here the benefits may outweigh the potential risks.
- A medicine that is to be used for a less severe and self-limiting disease, such as the common cold, would need to be far safer.

On the basis of decisions about their "risk profile", the MCC classifies medicines either as "prescription medicines" or "non-prescription medicines". A medicine does not need a prescription if the condition is self-evident and cannot be confused with a more serious condition, and is safe to use with minimal professional help. Some non-prescription medicines can be bought without a prescription from any general sales outlet. Others may be bought only from a pharmacist, but without a prescription. The pharmacist is expected to assess whether the medicine is needed, will be safe for that user, and also to provide the necessary information for the safe use of the medicine.

In contrast, medicines are classified as "prescription medicines" if professional involvement is needed to make the diagnosis, and to ensure safe use. Depending on the scheduling of the medicine, varying degrees of professional control or intervention by health professionals (such as pharmacists and doctors) will then be required.

## Ensuring quality

The quality of a medicine is assured by tight control of the manufacturing process – this is the time from the synthesis or collection of the raw material until the final packaging of the finished medicine.

There are two basic types of raw materials that form part of the manufacturing of a medicine. These are:

- *Active pharmaceutical ingredients (APIs)* – the chemicals that have an effect on the human or animal body.
- *Excipients* – pharmacologically inactive ingredients that are necessary to deliver the API to their desired place of action, for example: binding agents that allow tablets to stick together, sugars used to make syrups, preservatives, flavourings and colourings.

Extensive information about each of the manufacturing processes involved must also form part of an application for registration of a medicine. This includes information about:

- The stability of the active ingredient (the chemical substance).
- The final product in the packaged form in which it is to be sold.
- Different storage conditions such as temperature and humidity.

On the basis of this information, an approved time between manufacture and expiry of the medicine will be approved. This known as the shelf life and is shown by an expiry date for that medicine.

Key Point: Expiry date

No medicine should be used beyond the expiry date that appears on each package.

## Ensuring efficacy

The need for efficacy requires the applicant to submit data from the clinical trials conducted with the chemical. Clinical trial data are carefully examined to determine whether the expected benefit will in fact happen in clinical practice. On the basis of the trial data, the medicine will be recognised for a list of indications. These are the conditions or diseases for which it has been shown to be effective.

The experts reviewing a particular medicine will consider the balance between the medicine's risks and benefits. This will inform a decision on the "schedule" in the new medicine will be placed.

For more information on the different schedules, see 13.4 on page 428.

### Information for the public

The MCC, after recommendation by expert committees, certifies the exact wording of a package insert, with technical summary information, and the users' information leaflet, written in everyday language.

The package insert lists:

- The approved indications (uses) for the medicine.
- Basic details of the mechanism of action.
- The approved doses.
- Precautions and measures to ensure safety in normal usage and in overdose.
- The physical presentation of the product.
- Details of the registration number.
- Contact details of the holder of the registration certificate.

The package insert and user information leaflet are important sources of information for health professionals and consumers, and should always be accessible and understandable.

### Off-label use

Once a medicine is approved for sale, medical practitioners often prescribe it for other conditions. This is known as off-label use. Sometimes off-label use results in important discoveries about new uses for a medicine.

Perhaps the most important area of off-label use is in children. This is because doing research on children is very difficult, meaning that many medicines that are used in children have never been tested on them. This is particularly true of medicines used in the neonatal group (less than 4 weeks old).

Off-label use is not covered by the approved indications, but to make it illegal would deprive children of many useful medicines. As a result, medicine regulators across the world are trying to find ways to improve the quantity and quality of research done in children, and thus to register paediatric indications for as many medicines as possible.

### Registration procedures and issues

There are around 20 000 registered medicines in South African. Another 18 000 or more complementary medicines still have to be brought under effective regulatory control. As a result, the MRA cluster works under a lot of pressure, even though it has increased the size of its staff.

The application form, called the “MRF1”, for a new chemical is an extensive document, presented in a number of volumes. A total of 20 000 pages is not unusual. Much of the decision-making power rests with the MCC, not the secretariat. This means that a small group of part-time appointees must complete a large volume of work during their six-weekly meetings.

As a result, considerable delays in finalising applications for registration are common, with many applications taking more than two years to be processed. There is understandable concern about this delay, as it deprives people of access to useful new medicines, or more affordable generic medicines.

But there is also a concern that shortening the time to complete the registration process may lead to not fully considering the very real risks of potent chemicals. What is clear is that the MCC needs a bigger budget and more personnel.

#### Key Point: Careful registration and pharmacovigilance

In recent years, a number of new medicines have been found to have rare, but very dangerous side effects. An example of this has been Vioxx, a drug for arthritis. In 2004, this drug was withdrawn from the market worldwide after it was found to have contributed to heart attacks in a number of people. This has re-emphasised the need for an efficient registration process, but also for effective pharmacovigilance.

### Speedier registration

One way that delays can be avoided is to use a “fast-track” or speeded-up registration process. This is possible for medicines:

- on the *Essential Drugs List*; or
- deemed to be “essential for national health” by the Minister of Health.

For more on the Essential Drugs List, see 14.4 on page 458.

The company has to pay a double registration fee, but it is guaranteed an answer in nine months. The double fee is currently R25 000, compared to the usual R12 500 for each product.

“Fast-tracking” can take place in two ways:

- it can mean merely that the application “jumps the queue”, but has to be as complete as any other; or
- it makes use of Regulations to the Medicines Act that allow for a product to be registered using an abbreviated submission, but only if it has already been registered by another regulatory authority trusted by the MCC.

For more information on fast-tracking, see 14.4 on page 458.

### Registration of generic medicines

Like all inventions, medicines may be patented by their inventors. While a medicine is protected by a patent, only the holder of that patent may sell the medicine. The inventor may choose to license another firm to manufacture and sell the medicine.

When patent protection expires, anyone can make a copy of the medicine. This is called an “interchangeable multi-source medicine”, usually referred to as a “generic”.

Generic medicines still need to be registered, so data on the quality of the copy need to be submitted to the MCC. Generally, no new data on safety and efficacy are required – this does not mean that the generic medicine is any less safe or effective.

For more information on patenting and generic medicines, see 14.4 on pages 456–457.

### Re-examining registration and possible deregistration

Science and medicine are always evolving – what was known for a fact yesterday may well be proved wrong tomorrow. What was thought to be safe could well be proved to be unsafe, while what was thought not to be advisable may, on the basis of new evidence, be shown to be the preferred course of treatment.

Thus, each time the MCC makes a decision it is a judgment call – a decision based on weighing the available evidence. Later, the decision may be shown to be incorrect and a new decision, weighing new evidence of potential benefits and risks, may be needed. This is particularly true in a rapidly changing area such as the prevention and treatment of HIV.

Registration was in the past a one-off event – once registered, the medicine was not looked at again unless there was evidence of serious problems with the medicine. However, the Medicines Act was amended (by the Medicines and Related Substances Control Amendment Act 90 of 1997) to allow the Council to re-examine the registration status of all medicines every five years. If problems with the quality of a batch of medicines are discovered at any other time, then that batch may be recalled. This is done by manufacturers writing directly to every medical practitioner and pharmacist in the country.

If the MCC believes that it is no longer advisable for a medicine to be available to the public at all, it may deregister the medicine. Then all unsold stock of the medicine will have to be removed from the market and destroyed.

### Example: Removing a medicine

The cholesterol-lowering agent, Cerivastatin, was withdrawn worldwide in 2001 after being found to cause serious side effects.

### Unregistered use

There are two other circumstances under which “unregistered” medicines may be used. These are when a medicine is granted a “section 21 special approval” or if it is a personal prescription medicine from abroad.

### SECTION 21 SPECIAL APPROVAL

A section 21 approval is a special approval to import an unregistered medicine or purchase it from a company’s local agents. This happens if:

- a medicine that is not yet registered in the country needs to be used by an individual user; and
- there is sufficient information to support the choice on this medicine.

Section 21 approval can be also given to import or use unregistered medicines in clinical trials.

In all section 21 approvals, the idea is that the use is approved only for a limited number of users and for a limited period of time. If use becomes more widespread or is ongoing, the MCC will usually prefer the medicine to be submitted for full registration.

With all section 21 approval cases, the onus (duty) is on the doctor who has prescribed the medicine to monitor the safety of the user and to report any unwanted effects to the MCC.

### PRESCRIPTION MEDICINES FROM ABROAD

A second unregistered use is when a visitor to South Africa enters or a resident returns with a personal stock of medicines.

Approval here is limited to a month’s supply of Schedule 3 to 6 medicines (prescription medicines), and the person must be in possession of the original prescription or a certificate from the prescriber or dispenser of the medicine indicating that it was legitimately prescribed.

A draft amendment to the Medicines Act has been proposed that would allow residents leaving the country to carry a three-month supply, but would still allow only a month’s supply to be imported by returning residents or visitors.

### Appeal against decisions of the MCC

Any decision made by the MCC or the Director-General of Health can be appealed, as long as the appeal is made within 30 days of the decision.

The Minister of Health considers appeals against decisions by the Director-General. The Minister has to respond within a fixed time period. An appeal committee appointed by the Minister hears the appeals. The composition of the appeal committee has to be appropriate to the issues under discussion, but the chairperson is always someone chosen for his or her knowledge of the law.

Although the appeal committee may determine its own procedures, the time periods for finalising these appeals is also fixed. In addition, and particularly with appeals against decisions of the Minister, there is always the possibility of making an application to review a decision of the MCC through the High Court.

Example:

In 2005 the MCC rejected an application for a clinical trial intended to see whether the use of the anti-retroviral nevirapine by newborn babies being breastfed by HIV positive mothers, could reduce the rate of HIV infection through breast-milk. An appeal committee of the MCC overturned this decision, but the MCC still refused to give the trial a go-ahead. As a result the researchers approached the High Court and, in November 2006, won in an application to proceed with the trial.

## 13.4 Using medicines

Controlling the entry of medicines into the health care market is only one part of an effective system to protect the public. There is a need to also consider control of medicines in the marketplace, and control of the health professionals entrusted with particular powers in the marketplace.

### Scheduling of medicines

The Medicines Act lists substances in one or more “schedules”, based on their risk-benefit relationship. These lists match with the provisions of section 22A of the Act that sets out who may sell and buy medicines in each schedule.

We summarise the main characteristics of each schedule.

## Schedule 0 medicines

Schedule 0 medicines:

- Are generally safe and well understood.
- Are used in the treatment of conditions that can be easily identified by an ordinary member of the public.
- May be sold by anyone and to anyone.
- Are available in supermarkets and other retail outlets, without any professional involvement at all.

These medicines are sometimes called "over-the-counter", or OTC medicines for short. They must still be manufactured under controlled conditions in accordance with the standards set by the MCC. These standards are referred to as "good manufacturing practice".

Examples: Schedule 0

Aspirin and small quantities of paracetamol.

## Schedule 1 medicines

Schedule 1 medicines:

- Are also safe and well understood.
- Are made available only from pharmacies.
- May be sold only by a pharmacist, or a pharmacist intern or pharmacist's assistant under the supervision of a pharmacist.
- Should thus not be possible to select from an open shelf in a pharmacy.

No prescription is needed if the purchaser appears to be 14 or older. However, the person selling the medicine must also record various details of the sale.

Examples: Schedule 1

Antifungal creams, and some anti-bacterial and anti-inflammatory creams for application to the skin.

## Schedule 2 medicines

Schedule 2 medicines:

- Can also be bought without a doctor's prescription.
- Are considered to be "pharmacist prescription medicines".
- May not be advertised directly to the public, apart from notifying people about the price of the medicine in a particular strength and pack size.

The pharmacist selling the medicine must also record various details of the sale.

Only someone entitled to sell these medicines (a pharmacist or a holder of a dispensing license) may own Schedule 2 medicines for the purpose of sale.

Examples: Schedule 2

Most cold and 'flu preparations.

### **Schedule 3, 4, 5 and 6 medicines**

The public can get Schedule 3, 4, 5 and 6 medicines only with a prescription.

Various categories of prescribers are also provided for in the Act, including:

- Medical practitioners (doctors), dentists and veterinarians.
- Various types of allied health professionals (eg homeopaths).
- Nurses who are registered by their Council as competent to prescribe (eg primary health care and occupational health nurses).

As the Schedules increase in number (from 3 to 6), the conditions of sale and supply are tightened. There are specific restrictions on the extended prescription of some Schedule 5 medicines that have an abuse potential. Schedule 6 medicines are the most tightly controlled, as they have the most abuse potential. No repeat prescriptions for Schedule 6 medicines are allowed.

Examples: Schedules 3 to 6

Schedule 3: medicines for hypertension and diabetes.

Schedule 4: anti-infectives (eg antibiotics, antifungals and antivirals) and antiretroviral agents (eg zidovudine, nevirapine and lopinavir).

Schedule 5: psycho-active medicines (eg sedatives and antidepressants).

Schedule 6: narcotic painkillers.

Records of the purchase and sale of these medicines must be kept, with the greatest degree of control exercised over "specified Schedule 5" and Schedule 6 medicines. The specified Schedule 5 category is a sub-set of medicines that, together with the Schedule 6 medicines, are subject to international control measures by the International Narcotics Control Board (INCB).

### **Schedule 7 medicines**

Schedule 7 medicines are banned substances and cannot be sold by anyone.

Examples: Schedule 7

Cannabis, methaqualone (also known as mandrax) and heroin.

## Schedule 8 medicines

Schedule 8 medicines are a sub-set of a few Schedule 7 medicines that have a legitimate use in a very small number of cases. These are supplied directly from the Director-General of the NDoH to the doctor treating the particular health care user.

### Examples: Schedule 8

There are only three of these: amphetamine, dexamphetamine and nabilone. Each of these would be abused if not prescribed correctly, and they therefore remain listed in both Schedule 7 and Schedule 8.

## Control of health professionals

In each of the scheduled categories listed, we saw that control rests with a particular category of health professionals. This assumes effective control over these professions. In order to practise a particular health profession, a person must first be registered with a statutory body that controls that profession.

Health professionals are registered with these statutory councils, each under a specific Act of Parliament:

- *Health Professions Council of South Africa (HPCSA)* – registers doctors, dentists and a wide range of other professions, not all of whom have the right to prescribe medicines (eg psychologists, optometrists).
- *South African Pharmacy Council* – registers pharmacists, pharmacist's assistants, pharmacy students and interns.
- *South African Nursing Councils* – registers nurses, midwives and nursing assistants.
- *Allied Health Professions Council of South Africa* – registers a variety of complementary professions (eg homeopaths).
- *Interim Traditional Health Practitioners Council of South Africa* – registers various disciplines of traditional healers. Effective control of this category of practitioners and medicines is not yet in place, as the Act was passed only in 2004.

For more on the regulation of alternative and traditional medicine, see Chapter 7.

## Competence

The process of registration as a health professional involves submitting information that proves competence. This includes proof of completing a prescribed course of study at an approved institution (eg a Bachelor of

Pharmacy degree) *and* a prescribed period of practical training (eg a medical internship in an approved institution).

Most health professionals must also complete a period of “community service” in the public sector before they are allowed to practise in the private sector.

### CASE STUDY: DISPENSING LICENCES

Internationally, it is recognised that allowing all prescribers to dispense puts them in a position of “moral hazard”. This means that, instead of choosing the medicine best suited for a particular user, they may be tempted to choose only from what they have in stock, or to choose the medicine on which they may earn the most. Dispensing is also considered the specific competence of the pharmacist.

The Medicines Act allows prescribers (eg medical practitioners and nurses) to apply for a dispensing licence after completing a supplementary training course. In 2003, the legality of this provision was challenged by dispensing practitioners, who claimed that they had the right to dispense and that the government’s intervention was unreasonable.

This argument was eventually rejected by the Constitutional Court in the *Affordable Medicines Trust v Minister of Health* case (2004 (6) SA 387 (T)). The Court decided that:

- The regulations on dispensing were “in furtherance of the objective to increase access to medicines that are safe for consumption” (para 53).
- The Medicines Act gave wide powers to the Minister of Health to make regulations to further the objectives of the Act, including any measure to ensure the safety, efficacy and quality of a medicine.

The aim of the Medicines Act was that prescribers would be licensed only in settings where there was a demonstrable need – in other words, lack of access to registered pharmacists. However, this principle does not seem to have been applied in practice, and all applicants who have completed the supplementary training course have received their licences.

There are indications that this legislation will be amended before the current licences come up for review in 2008.

In addition to the legal requirements of the Medicines Act, each of the health professions is also subject to the control of its Act and Council, as well as the National Health Act.

### SCOPE OF PRACTICE

The process of registering health professionals also provides each profession with a *scope of practice* – a set of tasks for which that profession is deemed competent, and in some cases, only that profession is allowed to perform. However, there are circumstances where a degree of flexibility is needed, provided there is demonstration of competence and an element of control.

## Protecting health care users

### Licensing of health establishments

Health care users are also protected by legislative measures that control the premises where health care services are rendered. A number of health establishments involved in the supply and use of medicines are covered by licensing provisions.

Examples: Licensing

- Private hospitals and unattached maternity units are subject to legal standards and have to be licensed.
- The South African Pharmacy Council records the licensing status of all pharmacies and prescribes standards for the premises where pharmaceutical services are provided.
- The MCC has recently started licensing manufacturing and wholesale outlets, as well as importers of medicines.

Each of these processes provides another element of control and thus protects the rights of health care users.

### Rational use of medicines

One aspect that does not easily fit under legislative control is the *rationality* of medicine use.

The World Health Organisation has defined rational medicine use as: *“therapeutically sound and cost-effective use of drugs by health professionals and consumers”*.

In other words, *rationality* means that the user should receive the right medicine, at the right dose, at the right time, for the right duration, and at a cost that is affordable to the individual and the community.

The Medicines Act allows the MCC to consider the three elements – safety, quality and efficacy – when deciding on the registration of a medicine. How a medicine is used after this is largely an issue of professional choice.

However, it is also accepted that inappropriate prescribing reduces the quality of medical care and leads to a waste of resources. One way in which this can be avoided is to reduce the number of medicines available.

In South Africa, the DoH has implemented a policy of rational medicine use effectively in the public sector, where it has developed evidence-based Standard

Treatment Guidelines for the majority of conditions seen in the country. From these guidelines, it has been able to extract a smaller list of “Essential Drugs”.

Medical aid schemes have also started to follow the same process in the way that they design “formularies” or limited lists of medicines for which they are willing to pay.

### USER RIGHTS AROUND MEDICINE USE

In the use of medicine, consumers have a variety of rights that are entrenched in both the National Health Act and by the standards set by each of the statutory health councils.

In the table below we summarise four important consumer rights that are relevant to the use of medicines.

## 13.5 Conclusion

As this chapter has shown, medicines are subject to tight legal control. The reason for this is not the protection of the commercial interests of any of the actors in the distribution chain, but the safety of the public. This control extends from the very beginning of the process of developing a new medicine to the very last steps in the supply to and use by a health care user or client.

The basic approach for medicines and health professionals is registration

#### KEY POINTS: User rights

##### 1. The right to receive care from an identified and registered health professional

- Health professionals should display their registration certificates.
- Consumers should be able to determine whether the health professional they are seeing is competent and thus registered to provide the services.

This means:

- A pharmacist providing additional services, such as vaccination or the provision of family planning, should have special permission to do this.
- A prescriber who also dispenses medicine, should display a licence, obtained after completing the necessary supplementary training.

##### 2. The right to receive adequate counselling about the medicine supplied

- Health professionals, including pharmacists, should obtain informed consent from users, who, when a medicine is prescribed for them, should understand:
  - the reason for supply of the medicine
  - how to take the medicine properly
  - what side effects may be expected and what to do about them
  - how to store the medicine
  - who to contact if anything unusual happens or for more information.

with a statutory council. While the legal provisions that surround this system are complex, the rights they protect can be stated simply:

- The consumer has the right to expect that only safe and effective medicines will be allowed on the market.
- The consumer has the right to expect that only competent and registered health professionals, governed by effective codes of conduct, will provide health services. This includes all the steps involved in the prescribing and dispensing of medicines.
- The consumer has the right to access the necessary information to enjoy the safe and effective use of the medicine.
- People who choose to enrol in clinical trials have the right to the information necessary to make an informed choice, and also the right to withdraw from the trial at any time.
- At all times, whether as study participants, health care users or consumers, the rights to dignity and confidentiality must be protected.

For more on participating in clinical trials, see Chapter 12.

Medicines have the potential to make incredible contributions to the prevention and treatment of disease, but also carry considerable risks. These qualities make them different from ordinary articles of trade and require a system of protection to ensure the safety of the public.

- This right applies not only to medicines supplied on a prescription, but also to medicines bought over the counter in a pharmacy.

### **3. The right to exercise choices around generic medicines**

- The Medicines Act says that anyone dispensing a prescription (a pharmacist or a holder of a dispensing license) must offer the user a less expensive generic medicine if one is available.
- The prescriber may indicate that no substitution is allowed. The MCC also provides a list of non-substitutable medicines.
- The user always has the right to refuse the substitution of a patented medicine with a generic. If the user refuses the substitution, the dispenser must record this choice.
- If the user's insurer has appropriately approved "managed care" provisions in place (such as a reference price list), the user may be subject to a co-payment if refusing a lower priced generic medicine.

### **4. The right to confidentiality**

- Each of the statutory health councils says that all of those registered with it must respect the right of their users to confidentiality.
- The right to confidentiality is also recognised by the National Health Act.