

Pharmaceutical Innovation, Incremental Patenting and Compulsory Licensing Country Case Study: South Africa (Author Yousuf A Vawda).

1. Introduction

‘The roots of a dysfunctional health system and the collision of the epidemics of communicable diseases in South Africa can be found in policies from periods of the country’s history, from colonial subjugation, apartheid dispossession to the post-apartheid period. Racial and gender discrimination, the migrant labour system, the destruction of family life, vast income inequalities, and extreme violence have all formed part of South Africa’s troubled past, and all have inexorably affected health and health services.’ (Coovadia et al, 2009).

2. Health and medicines regime

South Africa is an upper middle-income country with an estimated population in mid-2010 of just under 50 million, with almost 80% being Black Africans. In the last Census (2001), 7.3% of the population was aged 60 years or older, and 32.1% was younger than 15 years. In 2008 the median age was 24 years. Between 2001 and 2010, the aging index (the the number of people aged 65 and over per 100 youths under age 15) had increased from 11 to 16, but was nearly 70 in the White population. By contrast, the ageing index in 2008 was highest in Western Europe (113) and Eastern Europe (97), and lowest in sub-Saharan Africa (7) and the Near East (14). (Day and Gray, 2010).

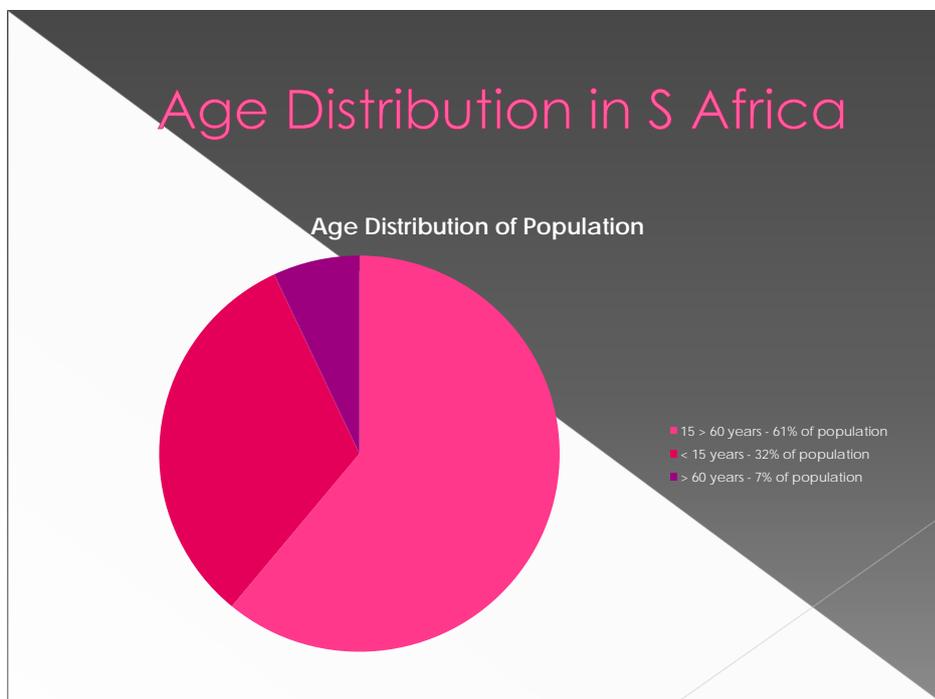


Figure 1: Age Distribution in S Africa (Adapted from Day & Gray, 2010)

According to this study, over 41 million South Africans did not have medical insurance in 2009, and were dependent on either the state or out-of-pocket payment for their health requirements. However, for those who are uninsured, all health services at primary health care facilities are free of charge, including medicines listed on the Essential Drugs List. In 2009, 74.4% of the White population was insured, compared with only 9.0% of the Black African population. The uninsured generally access healthcare services at clinics, community health centres and hospitals operated by the provincial and local authorities, but may also purchase services and products out-of-pocket in the private sector. Those who are insured would generally access healthcare services from private health practitioners, pharmacies and private hospitals. Despite the vast majority of the population being uninsured, the majority of health professionals practise in the for-profit private sector.

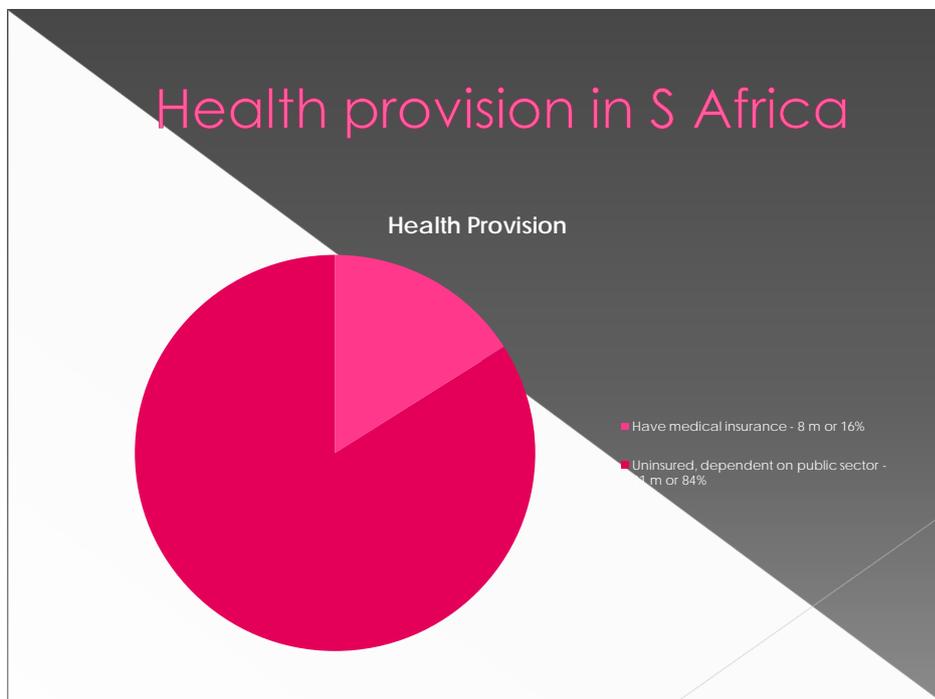
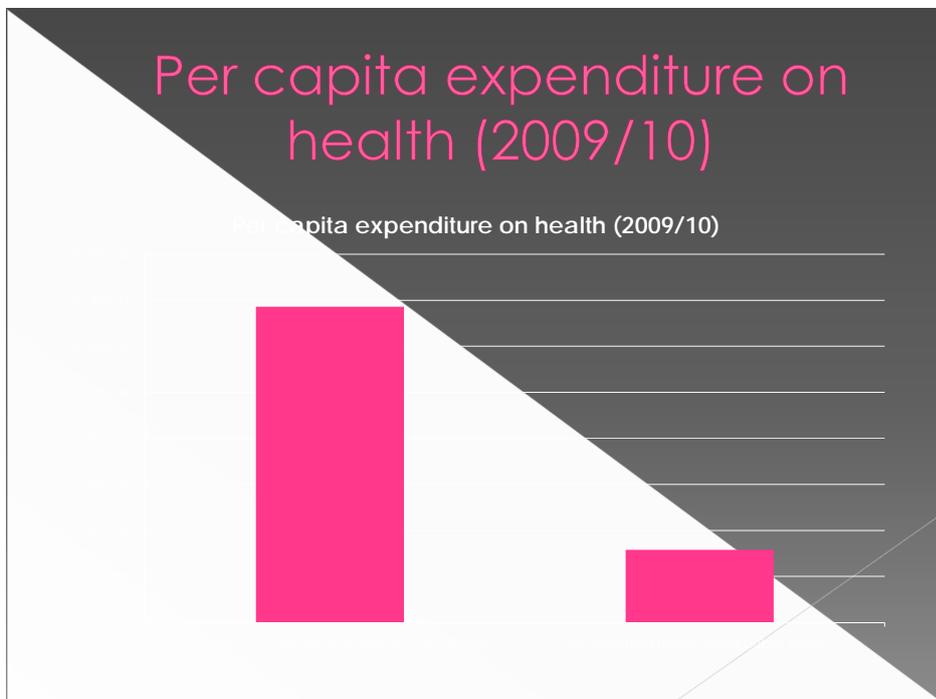
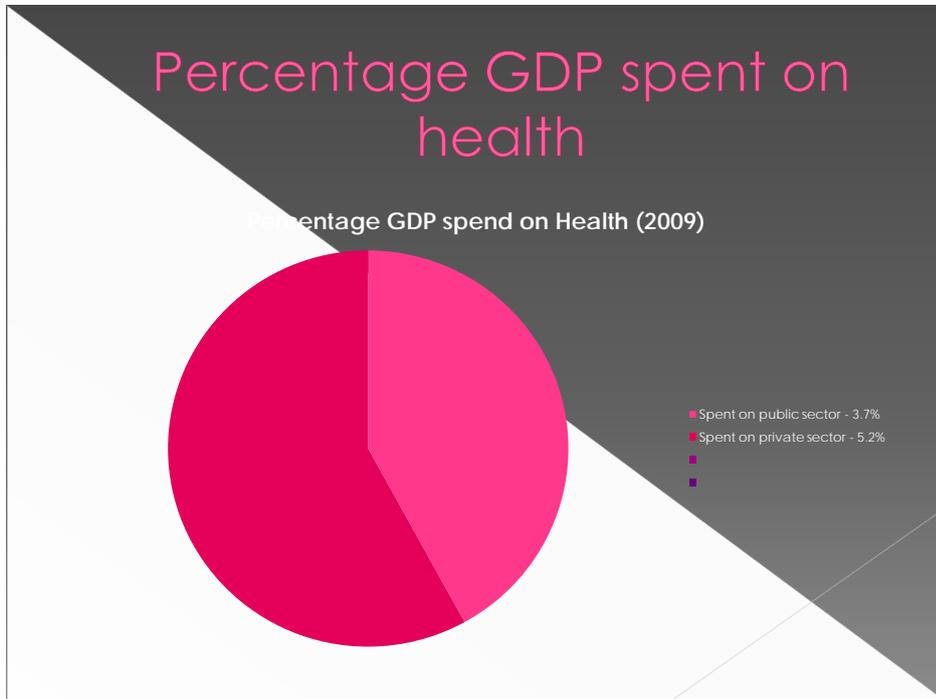


Figure 2: Health provision in South Africa (Adapted from Day & Gray, 2009).

South Africa confronts 'four concurrent epidemics' - HIV and AIDS, other infectious diseases, violence and injuries, and non-communicable diseases. Despite its middle-income status, it has health outcomes, such as child mortality, that are worse than many poorer countries (Coovadia et al., 2009). As the population ages, the burden of non-communicable disease is expected to increase (Mayosi et al., 2009). However, the health problems that have received the greatest attention, and for which access to affordable quality medicines is an imperative, are the linked epidemics of HIV and tuberculosis. South Africa has both the largest number of HIV-infected persons of any country and also the largest number on antiretroviral treatment (Abdool Karim et al., 2009).

In 2009, South Africa spent 8.9% of Gross Domestic Product (GDP) on health, made up of 5.2% expended in the private sector and 3.7% in the public sector. The per capita expenditure was ZAR9605 (approximately \$1372) per medical scheme beneficiary in 2009, compared with ZAR2206 (\$315) per uninsured person in the 2009/2010 public sector fiscal year.



Figures 3 & 4: Percentage GDP & Per capita (Adapted from Day & Gray, 2009).

3. Pharmaceutical market & production

South Africa has a large and highly developed pharmaceutical system, including considerable local production capacity. In October 2009, the South African Medicines Control Council licensed 221 entities as manufacturers, importers, and exporters of medicines (or in at least one of these categories). Of these, 76 entities were listed as manufacturers of medicines, meaning that some element of local production was involved. Of the total, 45 were locally-registered subsidiaries or offices of transnational pharmaceutical concerns, including the major American and European innovators in this field. While the majority of these were licensed as importers and exporters, some were licensed to manufacture locally and operated such plants. Of the balance, 13 were locally-registered subsidiaries or offices of international generic pharmaceutical manufacturers, including Teva, Sandoz and Ranbaxy. The remainder – 163 entities – were locally-based firms licensed to manufacture, import or export medicines. This excluded those operating exclusively as wholesalers or distributors of medicines. The oldest South African generic manufacturers have been operating in excess of 100 years and are major players in the local market, if not globally (Gray and Vawda, 2011).

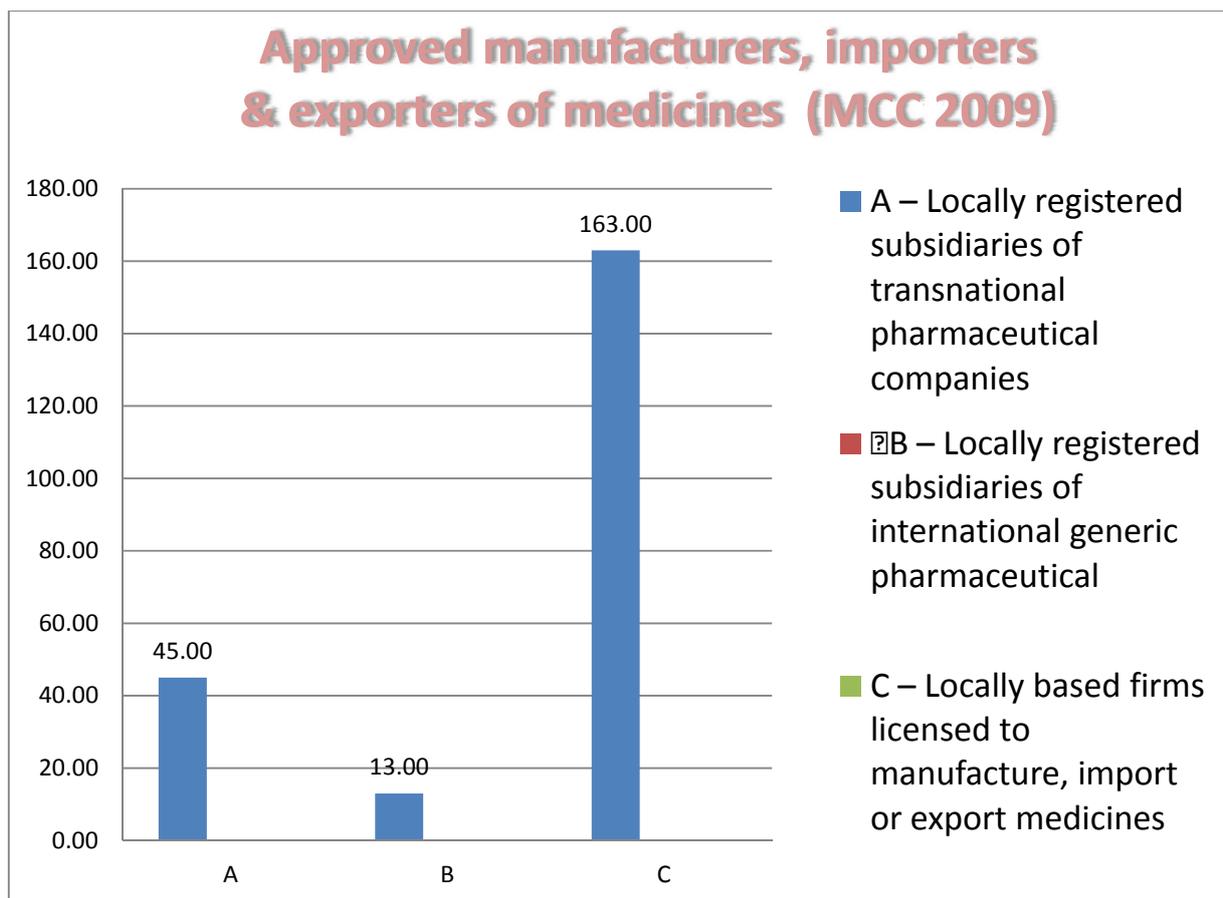


Figure 5: Approved manufacturers (Adapted from MCC, 2009).

However, a 2005 report on the issue of local production cited the view that the pharmaceutical industry in South Africa was then “small and not very wealthy”, as lacking “an ability to achieve economies of scale in production” (Kaplan and Laing, 2005). As expected, local research and development has largely been restricted to formulation issues, although there are new drug discovery projects in a number of public-private partnerships and in academic research centres.

Nevertheless, South African companies feature prominently in terms of pharmaceutical market share. The most recent statistics indicate that South African companies command a significant slice – 39% - of the local market (IMS Health South Africa, 2011). This is followed by the USA with 21%, Switzerland (11%), France (9%), Germany (7%), Great Britain (6%), Denmark and India (2% each), and Japan and Australia (1% each).

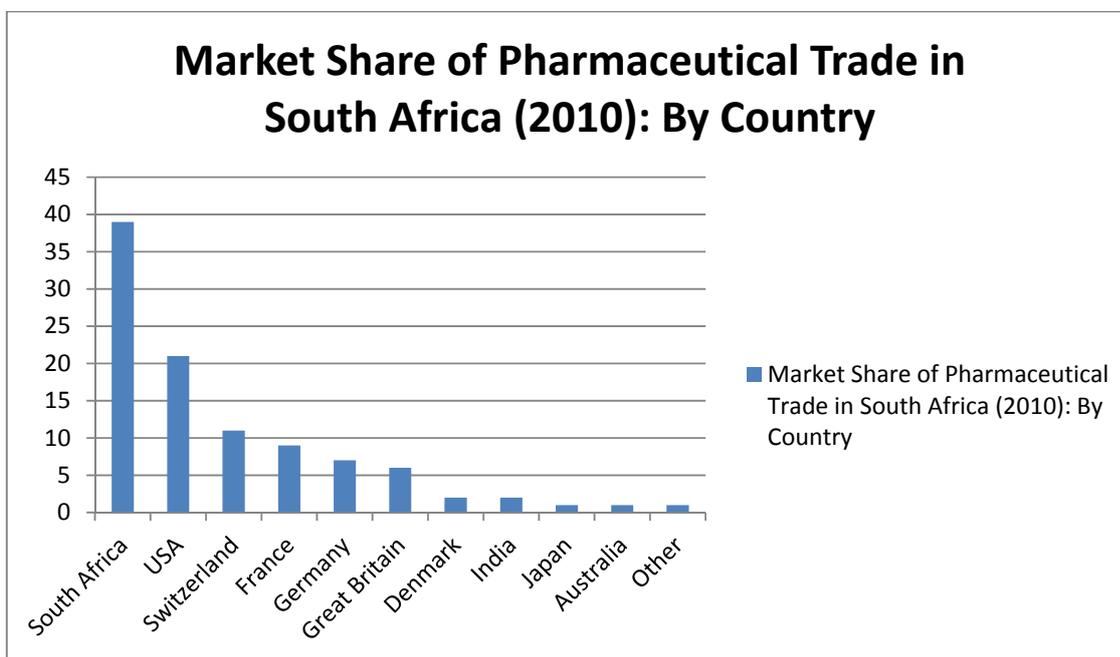


Figure 6: Market Share by Country (Adapted from IMS Health South Africa 2011).

Individually, two South African companies lead the suppliers of medicines in the country. Aspen Pharmacare commands 17% of the local market, and Adcock Ingram follows at 10%. The leading foreign companies are Sanofi-Aventis (France) and Pfizer (USA), each with 7%, Novartis (Switzerland) with 6%, followed by AstraZeneca (Great Britain) and Cipla Medpro (South Africa), each with 5% of market share. Others with significant presence in the market are Merck (USA) with 4%, Bayer (Germany) with 3%, and Abbott (USA) and Lilly (USA), each with 2%.

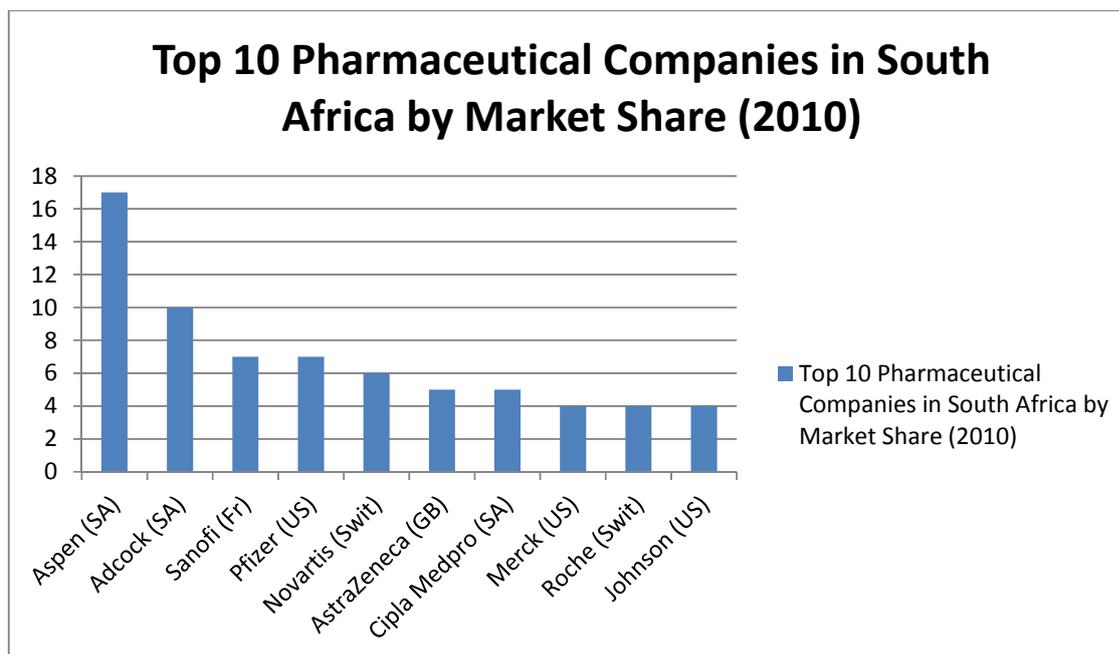


Figure 7: Top 10 Pharmaceutical Companies (Adapted from IMS Health South Africa 2011).

4. Medicines regulation

Medicines have to be registered by the Medicines Control Council (MCC), a statutory regulatory authority located within the national Department of Health (Gray, 2007). It is required to consider only issues of quality, efficacy and safety, and there is no linkage between patent status and regulatory approval. The enabling Medicines and Related Substances Act, No 101 of 1965 also provides for a degree of regulation of medicine pricing, exercised by the Minister of Health, as informed by a Pricing Committee (Gray, 2009). The Minister issues an annual maximum limit to increases for medicines sold in the private sector. The dispensing fees charged by pharmacists and other licensed dispensers are also regulated, and adjusted on an annual basis. An international benchmarking system, in which the prices of innovator products will be compared with those in a basket of countries, has been proposed but not yet implemented. In the public sector, medicines are procured in terms of centrally determined competitive bidding (tender) processes, limited to locally-registered products, and these are predominantly generics although some branded product are used (IMS Health, 2009). The 2010-2012 antiretroviral tender also introduced a benchmarking step, where indicative global best prices were provided before tenders were accepted. In this way, the public sector has been able to achieve competitive prices for first- and second-line antiretrovirals. However, the prices of newly-launched patent-protected medicines, generally brought to the market by transnational innovator firms, remain unregulated. Such medicines may not easily be included in the public sector Essential Drugs List, and may be refused reimbursement or attract considerable co-payments in the private sector (Gray and Vawda, 2011).

Since 2003, South Africa has used a requirement for mandatory offer of generic substitution to promote the use of lower-cost generic medicines. The trends in private sector medicines sales

over time are shown in Figures 8 and 9. In this categorisation, non-generic products are those that are patent-protected, original brands sold after patent protection has lapsed and first-launch products without patent protection. Generic medicines are approaching 50% of the private sector market share by volume and 30% by value. In the public sector, the limited Essential Drugs List contains predominantly older, off-patent medicines, and these are procured by tender, making substitution irrelevant.

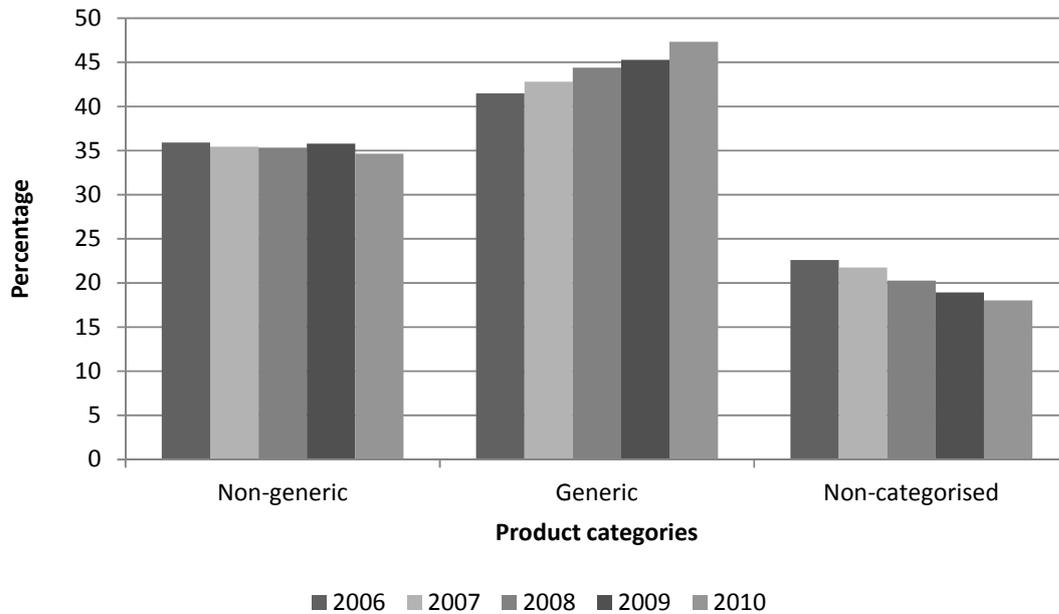


Figure 8: Percentage private sector market share by volume (IMS Health South Africa, 2010).

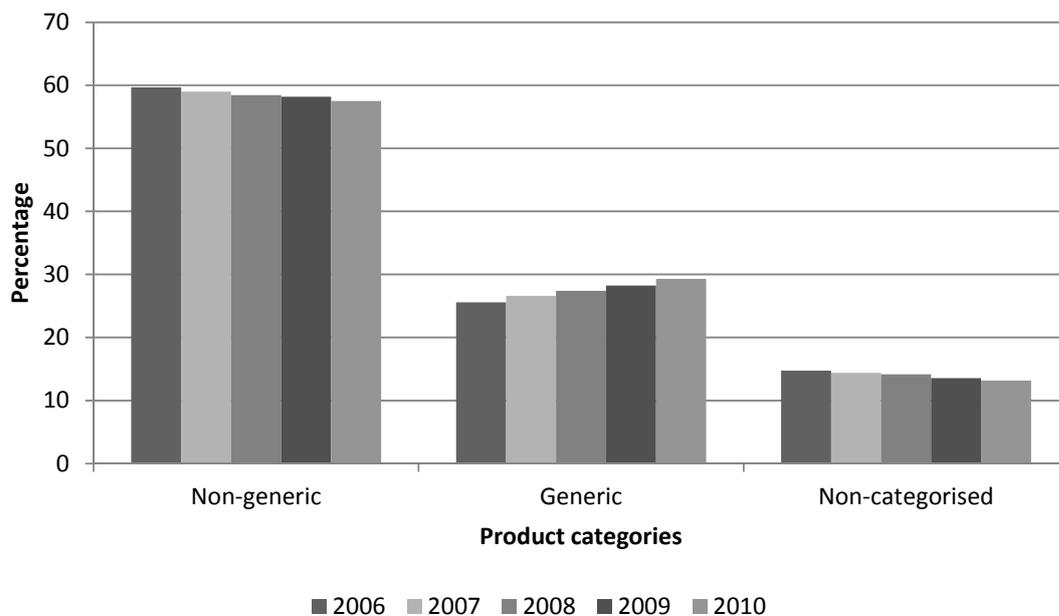


Figure 9: Percentage private sector market share by value (IMS Health South Africa, 2010).

5. Intellectual property protection in South Africa

5.1 Background

South Africa has had patent legislation since at least 1916, and the statute currently in force was promulgated in 1978 (Union of South Africa, 1916, Republic of South Africa, 1978). South Africa undertook to become TRIPS-compliant in 1997 (Republic of South Africa, 1997a), with the passage of the Intellectual Property Laws Amendment Act. South Africa also became bound by the Patent Co-operation Treaty in 1999 (Burrell, 1999). Further amendments to the Patent Act were made in 2002 and 2005 (Republic of South Africa, 2005, Republic of South Africa, 2002). While on the face of it, this appears to be a rational outcome of the process of patent harmonisation, it can also be viewed as further evidence of the extension of patent monopolies by simplifying the process of obtaining them in developing countries, and also of the process of negotiation which resulted in such agreements and treaties (Drahos and Braithwaite, 2004).

Compliance with the international intellectual property regime has come at great cost. Many developing countries have adopted the new intellectual property regime against their own best interests, and out of fear of inviting trade sanctions if they did not do so. Countries such as South Africa and Brazil attracted the wrath of the US when they adopted legislation which, in the view of the latter, used flexibilities in the TRIPS Agreement more broadly than the US wanted (Abbott, 2002, Bond, 1999). The 1997 amendments to the South African Medicines Act drew not only a legal challenge (Pharmaceutical Manufacturers' Association and Others v President of the Republic of South Africa and Others, case no. 4183/98, High Court of South Africa (Transvaal Provincial Division)), but also saw the US Trade Representative placing South Africa on its 301 Watch List, a precursor to sanctions. At about the same time, the US lodged a complaint with the WTO Dispute Resolution Panel against Brazil regarding its compulsory licensing legislation. The South African case was withdrawn under intense international scrutiny, and the complaint against Brazil was also withdrawn. However, such strong-armed tactics persist to the present day in trade negotiations between the developed and developing countries. South Africa has recently engaged in negotiations on a free trade agreement (FTA) with the US, through its participation in the Southern African Customs Union, and although the formal FTA talks have stalled, there are ongoing discussions on selected trade topics (Inside US Trade, 2006). As a result, many countries have adopted measures in their patent systems which go beyond that which is required by the TRIPS Agreement. An example of such measures is the heightened level of protection for clinical test data demanded by pharmaceutical manufacturers, which is not mandated by Article 39 of TRIPS, and which the US is routinely demanding be included in bilateral and regional trade negotiations.

South Africa's patent legislation already contains more stringent conditions than is necessary under international law (Republic of South Africa, 1978). Examples include the disclosure standards (section 32) and the process for compulsory licensing (section 56). Furthermore, it has not fully utilised provisions in its existing medicines law to take measures to improve the accessibility of medicines (such as the provisions to allow parallel importation), nor has it made the necessary legislative amendments consequent to the flexibilities provided in the Doha

Declaration and subsequent August 30 2003 Agreement (World Trade Organization Council for TRIPS, 2003, World Trade Organization, 2001).

Finally, the tension between the attainment of human rights (in particular, the right to access health care) and trade and intellectual property rules which impede the realisation of those rights, will not be resolved if medicines continue to be viewed as private items of consumption. It is increasingly being contended that medicines, already subject to a significant degree of regulation, must be construed as public goods because of their critical public health and public interest impacts (Parmet, 2006).

5.2 The Constitutional Framework

The post-apartheid South African Constitution contains several provisions dealing with socio-economic rights in general, and health rights in particular (Republic of South Africa, 1996). These include the right to access health care (section 27), bodily and psychological integrity (section 12(2)), privacy (section 14(a)), and to an environment that is not harmful to health or well-being (section 24(a)). In addition, the state must respect, protect, promote and fulfil the rights in the Bill of Rights (section 7(2)), including socio-economic rights. These obligations collectively mean that the state is required to not only refrain from the unfair and unreasonable curtailment of a person's rights, but also to take proactive measures to, for example, develop and implement a comprehensive legal framework for the realisation of those rights, and to create the necessary conditions under which individuals may be capacitated to themselves realise those rights. Most importantly, it provides that everyone has the right to have access to health care services, and that the state must take reasonable legislative and other measures, within its available resources, to achieve the progressive realisation of the right (sections 27(1) and (2)).

The right is, however, subject to two important qualifications, namely, that it must be progressively realised, and that it is subject to available resources. The leading decision on the issue of access to medicines is undoubtedly the TAC case (*Minister of Health & Others v Treatment Action Campaign & Others* 2002 (5) SA 721 (CC) and *Minister of Health and Others v Treatment Action Campaign and Others* (no 2) 2002 (5) SA 717; 2002 (10) BCLR 1033 (CC)). Firstly, the judgment affirmed the centrality of access to medicines in the realisation of the right of access to health care. Secondly, it recognised that constraints on the public purse are not necessarily an impediment to the realisation of rights. Thirdly, the Court stood firm on the challenge to its authority to make pronouncements on policy matters, in various guises, notably under the 'separation of powers' doctrine. It recognised that disputes over socio-economic rights invariably required the evaluation of state policy and an order for 'appropriate relief' where such policy is inconsistent with the Constitution, which could include mandatory orders and supervisory jurisdiction or structural interdicts. Finally, the decision elaborated the understanding of the concept of 'progressive realisation of rights' as not merely signifying 'pious wishes' but entailing a serious commitment to the delivery of health care services (Mathipa and Budlender, 2002).

The TAC decision has paved the way for a significant access-to-medicines jurisprudence, and in its wake, a number of critical questions arise in relation to intellectual property provisions in the law:

- Given the high costs of antiretrovirals (ARVs), would the measures necessary to contain the HIV/AIDS pandemic include the issuing of compulsory licences to facilitate the manufacture and importation of cheaper medicines?
- Is this interference with the rights of pharmaceutical patent holders constitutionally tenable? Or does it violate their protected private property interests (defined in section 25)?

In trying to decide whether issuing compulsory licences is reasonable, the intent of the legislature might be a guide. These measures were included in patent law precisely to making inventions (including medicines) accessible, for example in the event of abuse of patent. South Africa also has competition legislation, the Competition Act which permits divestiture as a remedy for anti-competitive practices. In addition, section 15C of the Medicines and Related Substances Act allows the Minister to enable parallel importation in order to facilitate affordable access to medicines. (and other products) more affordable. The test of reasonableness entails a balancing of interests, the public interest served by saving lives taking precedence over the private commercial interests of the patent holder. Should there be a conflict between the right to health and private property protection, “constitutional right will always trump policy” (Davis, 1992). This principle has also been tested in law (*Ex parte* Chairperson of the Constitutional Assembly: *In re* Certification of the Constitution of the Republic of South Africa 1996 (4) SA 744 (CC)).

5.3 Components of South Africa’s patent regime

Compliance with the TRIPS Agreement required relatively few, though critical, amendments in 1997. The key relevant features of the patent regime are recounted below.

Patent standards

The Patents Act provides that a patent “may be granted for any new invention which involves an inventive step and which is capable of being used or applied in trade or industry or agriculture” (section 25(1)).

Novelty

Novelty requires that the invention be new, namely, that it has not previously been described (usually in writing) or widely used. As regards this requirement, the Act states that “an invention shall be deemed to be new if it does not form part of the state of the art immediately before the priority date of that invention” (section 25(5)).

Inventiveness

An invention is deemed to involve an inventive step “if it is not obvious to a person skilled in the art” having regard to any matter already available to the public (section 25(10)). In other words, it must be a step beyond routine discovery, or more than the mere adding together of previously known products or processes (for example, *Gentiruco AG v Firestone SA (Pty) Ltd* 1971 BP 58 (A) 172) and that “the objection based on a lack of inventiveness is one of long standing in our patent law” (*Ensign-Bickford (South Africa)(Pty) Limited and Others v AECI Explosives and Chemicals Limited* 1998 BIP271 (SCA) 281).

New uses of an invention

Having considered the parameters of what is patentable, the question which arises is: In defining patentability criteria in respect of medicines, should new uses of the invention (other than its originally intended use) or new forms (for example, use in paediatric as opposed to adult therapy) be excluded from patentability? Would such instances constitute novelty and an inventive step? In general, the position South African courts have adopted is that once a substance forms part of the state of the art, a new or second use thereof will not make it eligible for a new patent (Burrell, 1999). This interpretation is consistent with the relative freedom countries are accorded to opt for higher standards for the requirement of inventiveness (United Nations Conference on Trade and Development (UNCTAD) - International Centre for Trade and Sustainable Development (ICTSD), 2005). India is a good example of how this flexibility has been utilized, where section 3(d) disallows the patenting of a new form of a known substance which does not result in enhanced efficacy, or a new use of a known substance or process (Republic of India, 2005). However, as South Africa does not have an examination system for patent applications, the appropriate standard is not likely to be observed, unless subjected to a legal challenge through revocation or infringement proceedings (such as in *H Lundbeck A/S & Another v Cipla Medpro (Pty) Ltd* 2008 BIP 79).

Industrial applicability

The requirement that the invention must be one “which is capable of being used or applied in trade or industry or agriculture” (section 25(1)) resonates with that of utility found in many jurisdictions. South African courts have held that ‘useful’ bears the ‘special meaning of effective to produce the result aimed at’ or promised (Burrell, 1999). In other words, to be ‘useful’ any suitably knowledgeable person following the specifications of the patent must be able to make the invention.

Disclosure

The South African equivalent of the disclosure provision spells out the contents of a specification in some detail, requiring an abstract; a sufficient description illustrating or exemplifying the invention and the manner of performance; and the claim(s) defining the invention, which have to be clear and fairly based on the matter disclosed in the specification (sections 32(3) and 32(4)).

Opposition procedures

South African legislation makes no provision for opposition procedures, limiting the examination of applications and specifications to the Registrar of Patents, who is empowered to grant the application if it complies with the requirements of the Act (section 34). However, inspection by the public is permitted after the patent has been sealed and granted.

Furthermore, there appears to be a complete lack of transparency in the patent processing process, as the statute merely requires the registrar to conduct a formal tick-box approach to an application (section 34). Given that patent grants, particularly in the case of essential medicines, have such far-reaching impacts on the broader public, the process ought to accommodate public scrutiny and comment. Perhaps the best method of achieving this participation is through the opportunity to file a pre-grant opposition. Once again, the Indian experience is instructive, where

sections 25(1) and 25(2) of the Indian Patent Act provide for both pre- and post-grant opposition (Republic of India, 2005).

Exclusions from patentability

South African legislation covers most of the exclusions envisaged by TRIPS Article 27, namely, inventions which encourage offensive or immoral behavior (section 25(4)(a), any plant or animal variety or any essentially biological process for their production excluding a microbiological process or its product (section 25(4)(b)), as well as any surgical, therapeutic or diagnostic method of treatment of humans or animals (section 25(11)). Furthermore, the Patents Act empowers the Registrar of Patents to refuse any application that is frivolous; or whose use encourages illegal, immoral and offensive behaviour, including publication or exploitation (section 36). As the concepts of morality and offensive behaviour are relative concepts, particularly in a diverse and evolving society such as South Africa, it is unclear how this provision is to be applied.

Exceptions

There is no general provision in South African law of the order of Article 30 of TRIPS, but through its provisions relating to infringement, the Patents Act specifies two instances of exceptions: the use of patented inventions aboard convention vessels, aircraft or land vehicles temporarily or accidentally within territorial waters or in the Republic, and the making, use, exercise, disposal, offer to dispose and importing of the patented invention for purposes of obtaining regulatory approval for the manufacture, production, distribution, use or sale of any product (sections 69 and 69A of the Patents Act). The latter, Bolar-type exception, allows a generic producer, seeking to register a follow-on equivalent of a previously approved or registered medicine, to begin product development and compilation of the required registration dossier even before a patent has expired.

South African legislation is, however, lacking to the extent that it makes no provision for educational, experimental and research exceptions, nor for the export of an invention manufactured on a non-commercial scale in pursuance of the early working exception.

Compulsory licensing

The Patents Act permits the granting of compulsory licences under two broad categories: for dependent patents (section 55) and in instances of abuse of patent rights (section 56). The latter is of more direct significance to access to medicines. It sets out four circumstances under which patent rights are deemed to be abused, namely:

- If the patented invention is not being worked in the Republic on a commercial scale or to an adequate extent.
- If the demand for the patented article in the Republic is not being met to an adequate extent and on reasonable terms.
- If the refusal of the patentee to grant a licence on reasonable terms prejudices trade, industry or agriculture.
- If the demand in the Republic for the patented article is being met by importation and the price is excessive compared to the price in the country of manufacture.

No compulsory licences have to date been granted on pharmaceutical products in South Africa although there is a handful of reported decisions on the issue. For example, the Supreme Court of Appeal rejected an application for a compulsory licence on the grounds of abuse of patent, being non-working and failure to license (*Syntheta (Pty) Ltd v Janssen Pharmaceutica NV & Another* 1999 (1) SA 85 SCA) on the grounds that the applicant had not placed sufficient information before it to establish the abuse alleged.

Finally, on the issue of compulsory licences, South African law has not incorporated the important flexibility contained in the Doha Declaration facilitating such licences for public health emergencies.

Government use

Section 4 of the Patents Act provides that “a Minister of State may use an invention for public purposes on such conditions as may be agreed upon with the patentee, or in default of agreement on such conditions as are determined by the commissioner on application by or on behalf of such Minister and after hearing the patentee”. Further, section 78 states that “The Minister may, on behalf of the State, acquire, on such terms and conditions as may be agreed upon, any invention or patent”. Under section 25(2) of the Constitution, the government could also ‘take’ or expropriate the patent subject to just compensation.

Voluntary licences

In South African law, a voluntary licence is an “authorisation given by a patentee to another to invade the patent monopoly with impunity” (Burrell, 1999). A voluntary licence may take one of three forms: non-exclusive (where the patentee may still grant licences to others); exclusive (all others, including the patentee, are excluded); and sole (all others, with the exception of the patentee, are excluded) (Burrell, 1999).

The best-known cases of voluntary licences in respect of pharmaceuticals are those granted as part of the settlement of the Competition Commission complaint against GlaxoSmithKline and Boehringer Ingelheim, in favour of local companies (*Hazel Tau & Others v GlaxoSmithKline & Boehringer Ingelheim* (Case no. 2002Sep226)). Although subsequent applications by generic manufacturers for voluntary licences on other antiretrovirals were successful, this was not always the case (Avafia et al., 2006).

Parallel importation

South African law recognises the doctrine of exhaustion, although the Patents Act did not make explicit provision for it until recently. It had been left to the judiciary, drawing on the jurisprudence of the UK and the USA, to enunciate the rules governing exhaustion (*Stauffer Chemical Co v Agricura Ltd* 1979 BP 168 (CP)). The 2002 amendments to the Patents Act saw the introduction of a provision permitting parallel importation (Republic of South Africa, 2002). Furthermore, the 1997 amendments to the Medicines Act expressly introduced a provision authorising the Minister of Health to remove patent protection on medicines put on the market by the owner or with his consent, effectively permitting parallel importation (Republic of South Africa, 1997b). As to whether this included the importation of generic medicines legitimately produced under a compulsory licence became the subject of the litigation by the pharmaceutical industry against the government. This issue was settled by the promulgation of regulations, which specify the conditions under which parallel importation may take place. Another grey area is whether the TRIPS Agreement requires parallel importation to be limited to patented products,

and indeed, Kenya's 'liberal' provisions in this respect appear to have passed muster with the TRIPS Council review for compliance (Lewis-Lettington and Banda, 2004).

Revocation of patent

The issue of revocation has particular currency in the South African context, given that patent applications are not subjected to examination and scrutiny as to their merits. The Patents Act makes provision for patents to be revoked on the grounds of ineligibility of the patentee, patent granted in fraud of another's rights, non-patentability of the invention, inability of performance of the invention as illustrated in the specification, incompleteness of the method of performance, claims in the specification not being clear or not fairly based on matter disclosed, intentionally false representation in the application, frivolity or offensive or immoral use of the invention or claims of a microbiological process or product as an invention (section 61(1) and where a patentee makes a false declaration as to the origin of indigenous biological resources and his or her authority to use same (Republic of South Africa, 2005).

The grounds available are signally ones that relate to a fraudulent act, mistake, or non-disclosure of complete specifications. What is conspicuously lacking is the possibility of revocation in the case of abuse of patent, as provided for in Article 5A of the Paris Convention on Intellectual Property of 1883.

5.4 Competition law

The exercise of intellectual property rights, to the extent that they create monopolies, may give rise to anti-competitive behaviour either by individual companies, or through collusive activity. Competition law and policy as a strategy to access medicines is a relatively new development in South Africa. In at least one Competition Commission ruling, innovator companies have been found to have engaged in anti-competitive conduct, and thereby abused their patents, by charging excessive prices and denying a competitor access to an essential facility (Hazel Tau case). Competition law thus provides another effective sanction against patent abuse in the form of an anti-competitive compulsory licence, which is consistent with Article 31(k) of TRIPS and is, further, not subject to the domestic use and prior negotiations requirements.

5.5 Data protection

Protection of clinical trial data in South Africa predates its inclusion in the TRIPS Agreement, which requires that undisclosed clinical trial data must be protected against unfair commercial use and disclosure (Article 39). In line with the practice of regulatory authorities worldwide, the Medicines Control Council (MCC) does not publicly disclose or share data submitted for registration purposes. However, when considering an application for the registration of a generic equivalent, the MCC does not require the applicant to furnish any new data on the safety and efficacy of the drug, but merely on the quality of the generic (Gray, 2007). Data presented before is not directly accessed or cross-referenced, but exemption from providing such data is allowed. There is no obligation on members to grant exclusive rights over data, as is the case in the US, the EU and other countries (Correa, 2006). The effect of such protection is that generic producers are "precluded from relying on pre-existing data to establish safety and efficacy even when the producer has evidence that the two drugs are bioequivalent." (Druce et al., 2004)

The issue of data protection has gained greater prominence because of its inclusion in Free Trade Agreements. Many FTAs require the parties to grant data exclusivity rights for a minimum of 5 years irrespective of whether a patent is issued or not, or whether the invention is undisclosed or not. Following the collapse of the FTA negotiations between the US and the Southern African Customs Union (SACU) the pressure to adopt stringent data exclusivity rules has eased (Vawda, 2007).

In keeping with the imperative to incorporate all available flexibilities in the international intellectual property and regulatory regimes to advance the agenda of universal access to medicines, South Africa should legislate to secure the MCC's right to rely on the innovator's data when considering applications for generic medicines without direct cross-reference to such data. Public health interest demands that data protection be limited strictly to the parameters outlined in Article 39.3 of TRIPS.

5.6 Concluding Comment on the Intellectual Property Regime

The changes introduced in South Africa's law as a result of TRIPS thus included, in the main, the extension of patent protection for a period of twenty years (previously sixteen years); and the removal, as a ground for compulsory licensing, of the situation where the commercial working of an invention was being hindered by importation of the patented article. Also introduced were provisions for the use of the regulatory early working exception, the deletion of the requirement of disclosure of the best method of performing the invention known to the applicant at the time the application is lodged, and the lowering of the disclosure standard further by amending the requirement for the specification to be 'fully' described to 'sufficiently' described. Significantly, a provision has been introduced to effectively permit parallel importation.

Nonetheless, important flexibilities have not been incorporated in the legislation, notably those relating to compulsory licences for public health purposes, strictures on patenting standards, provisions for the use of the Paragraph 6 Decision; educational, research and experimental exceptions to patent rights, increasing the grounds for revocation of patents; and provision for opposition procedures to patent applications both before and after grant. In all these respects, the legal framework for intellectual property protection in South Africa can still be improved to considerably enhance access to medicines. While free trade negotiations in which South Africa was a participant have stalled, this potential threat to a pro-access intellectual property system still exists. South Africa can expect to come under increasing pressure to provide linkages between patent status and medicines regulatory practice and also to increase data protection measures.

6. Analysis of the Pharmaceutical Patent Database

The South African Patent Journals for 2008 were searched, and some 2442 pharmaceutical patents identified and entered into the database. This data is now analysed according to key variables.

Distribution of pharmaceutical patents by type (2008)

Of the pharmaceutical patents identified in the year 2008, 1426 (58%) were for products, 445 (18%) for product and process, 228 (10%) for process, and 343 (14%) were unspecified.

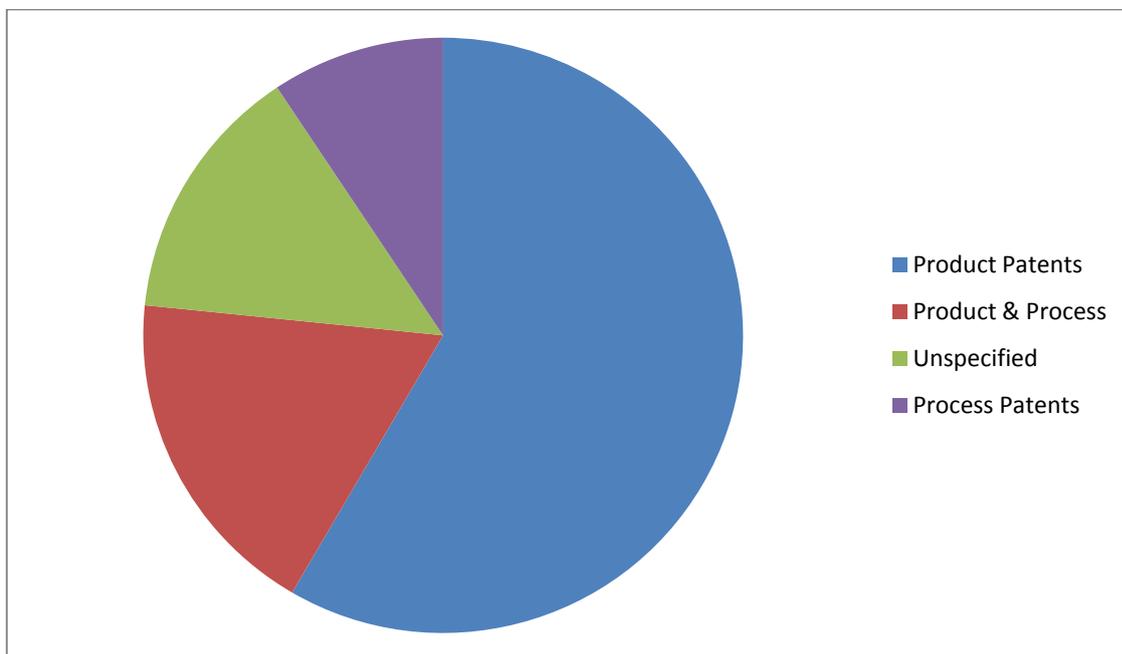


Figure 10: Distribution of patents by type.

Distribution of pharmaceutical patents by therapeutic class

Of the selected group, 445 (18%) were for Antineoplastic and immunomodulating agents, 325 (13%) for Nervous system, 308 (13%) for Anti-infectives for systemic use, 173 (7%) for Alimentary tract and metabolism, 151 (6%) for Cardiovascular system, 111 (5%) for Musculo-skeletal system, 81 (3%) for Genito-urinary system and sex hormones, 76 (3%) for Respiratory system, 63 (3%) for Blood and blood-forming organs, 46 (2%) for Dermatologicals, 33 (1%) for Sensory organs, 19 (0.7%) for Various classes, 18 (0.7%) for Systemic hormonal preparations, excluding sex hormones and insulins, 6 (0.1%) for Anti-parasitic products, insecticides and repellants, and 587 (24.5%) were unspecified.

Distribution of patents by type of claim, including Markush Claims

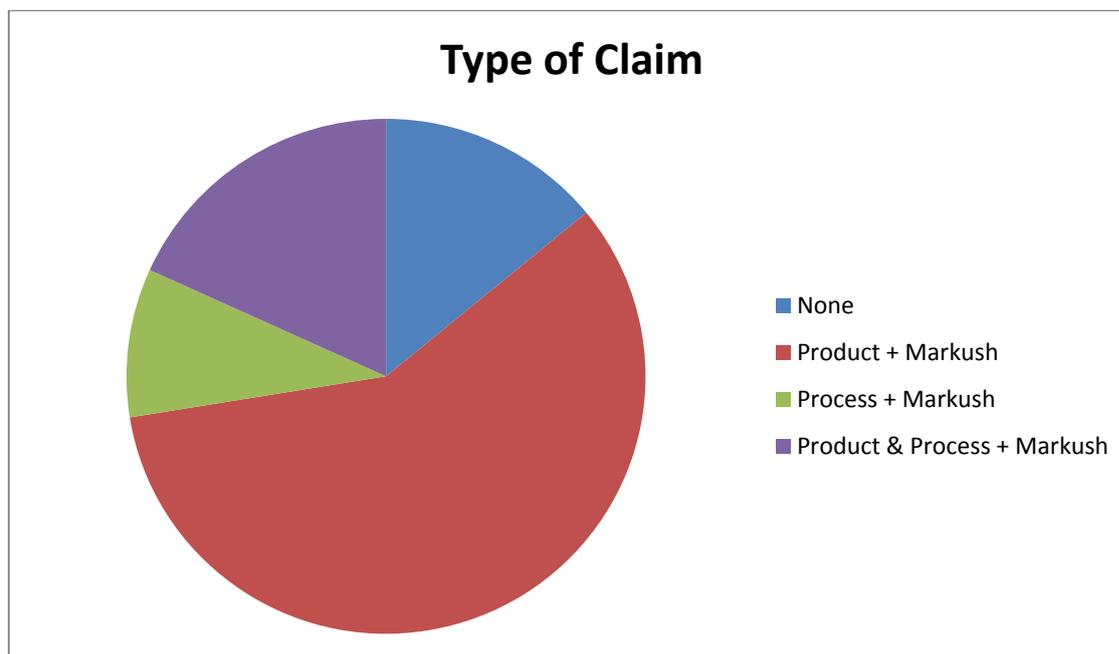


Figure 11: Distribution of patents by type and Markush Claims.

Distribution of patents by therapeutic use

Anti-neoplastic & immunomodulating agents	445
Nervous system	325
Anti-infectives for systemic use	308
Alimentary tract & metabolism	173
Cardiovascular system	151
Musculo-skeletal system	111
Genito-urinary system & sex hormones	81
Respiratory system	76
Blood & blood-forming organs	63
Dermatologicals	46
Sensory organs	33
Various	19
Systemic hormonal preparations excluding sex hormone & insulin	18
Anti-parasitic products, insecticides & repellants	6
Unspecified	587

Table A: Distribution of patents by therapeutic use.

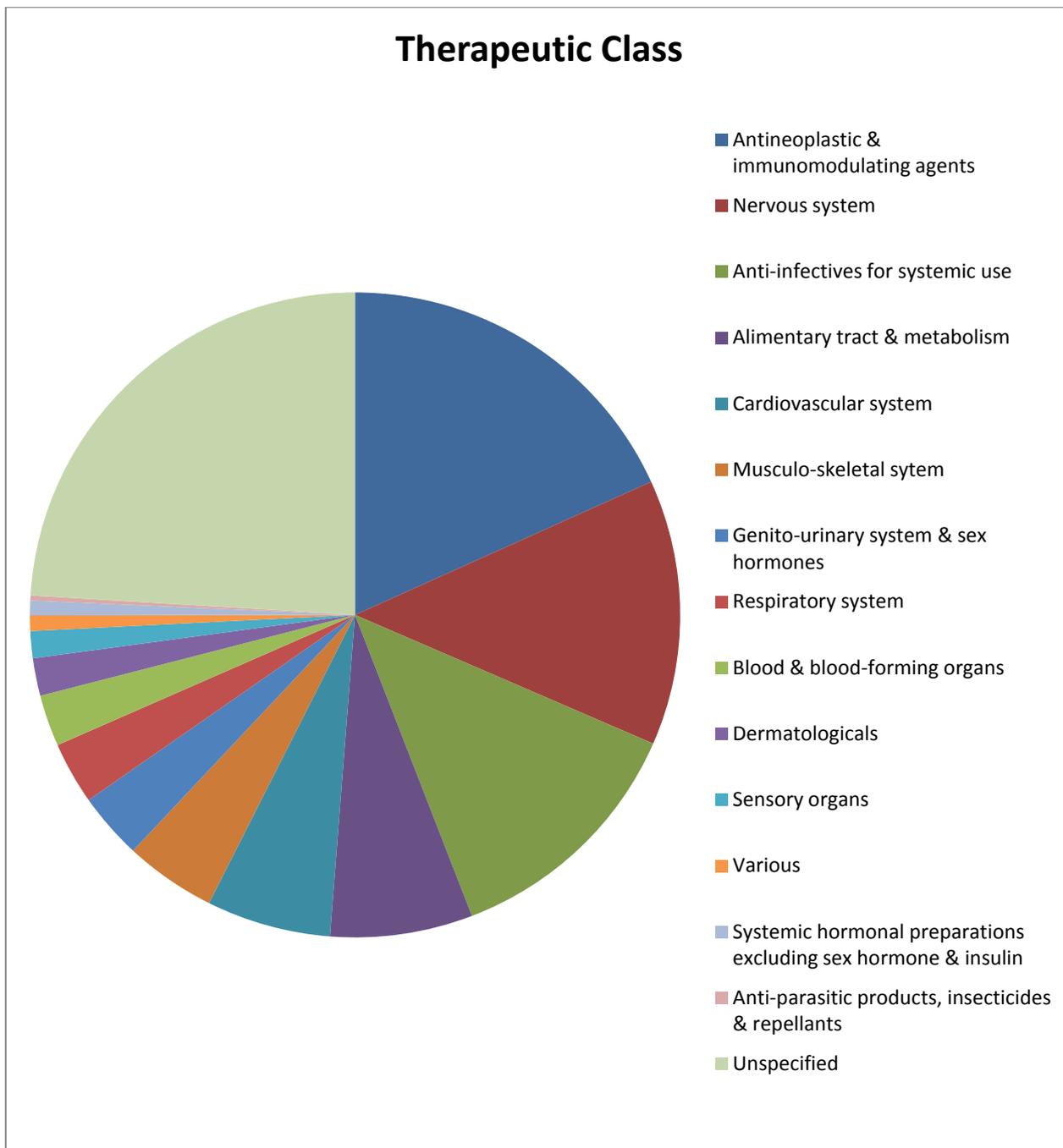


Figure 12: Distribution of patents by therapeutic class.

Patents held by companies by country of origin

The USA was the leading country of origin for the patents with 1208, followed by the UK 234, Germany 166, France 107, Japan 83, Switzerland 82, Sweden 80, India 59, Denmark 51, Netherlands 34, Italy 26, South Africa 16, China 12, and Brazil 1. Country of origin was not identifiable in 137 cases.

COUNTRY	ORIGIN	NUM	%AGE
South Africa	United States	1208	49
South Africa	United Kingdom	234	10
South Africa	Germany	166	7
South Africa	None	146	6
South Africa	France	107	4
South Africa	Japan	83	3
South Africa	Switzerland	82	3
South Africa	Sweden	80	3
South Africa	India	59	2
South Africa	Denmark	51	2
South Africa	Netherlands	34	1
South Africa	Italy	26	1
South Africa	South Africa	16	1
South Africa	China	12	0.5
South Africa	Brazil	1	0.05

Table B: Holders of South African patents by country.

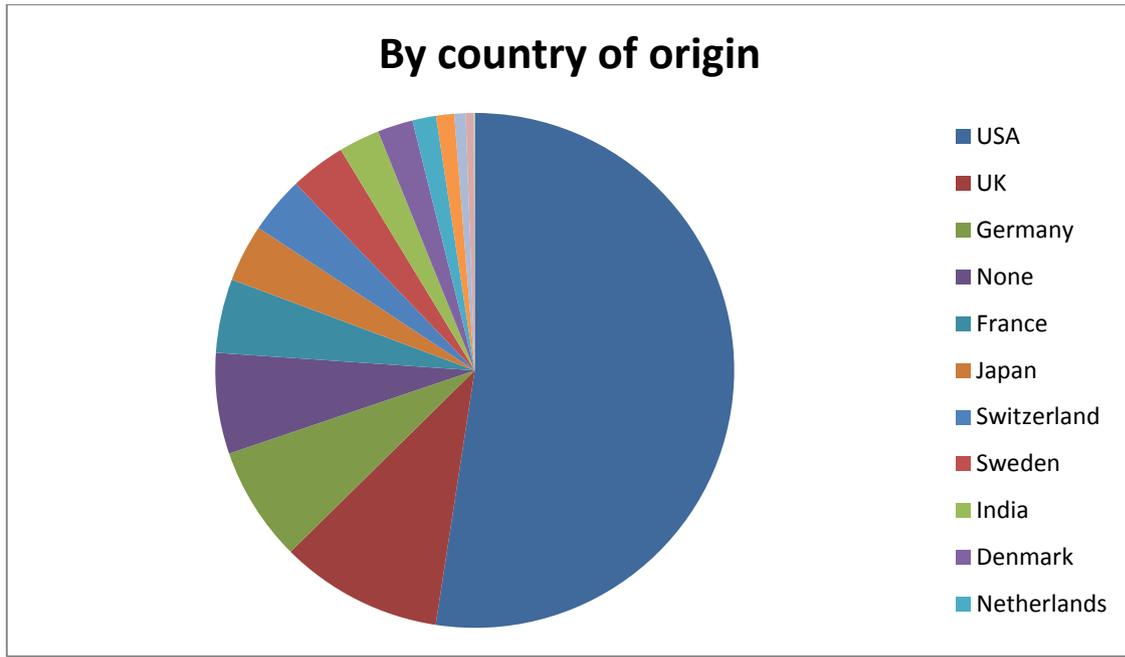


Figure 13: Holders of South African patents by country of origin.

Distribution by type of patent for leading countries

The USA is the leading country of origin for the majority of patent holders.

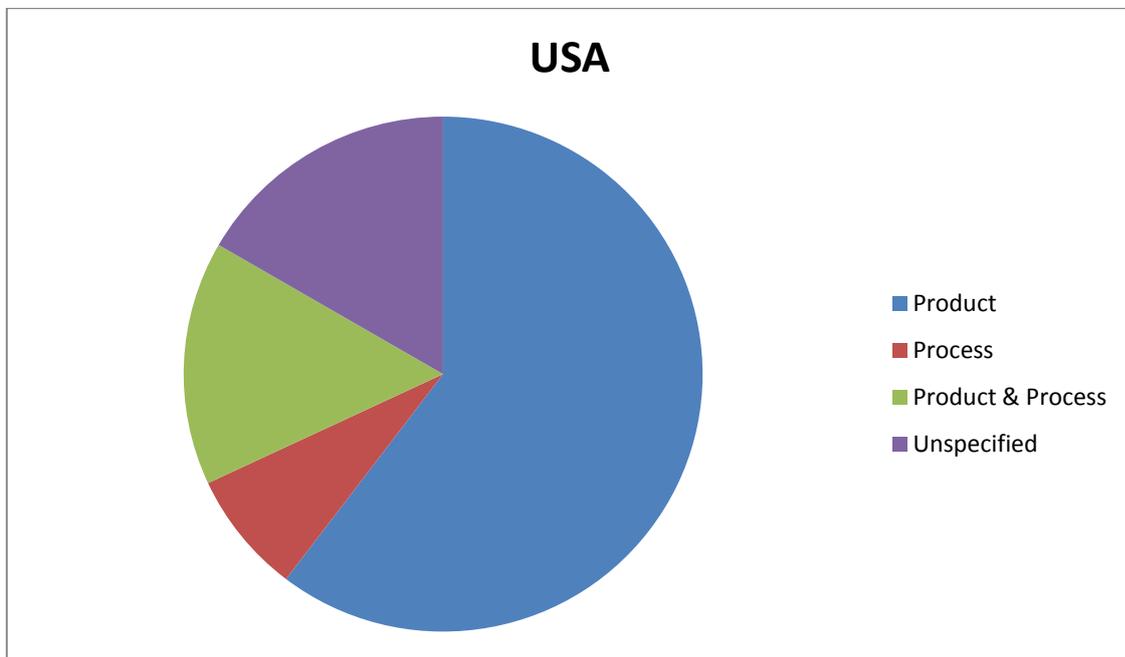


Figure 14: Patents held by US holders, by type.

Of the 1208 patents held by US companies, 729 (60%) were for products, 93 (8%) for process, 185 (15%) for product and process, and 201 (17%) were unspecified.

A similar pattern emerges in respect of patents held by United Kingdom holders of patents registered in South Africa.

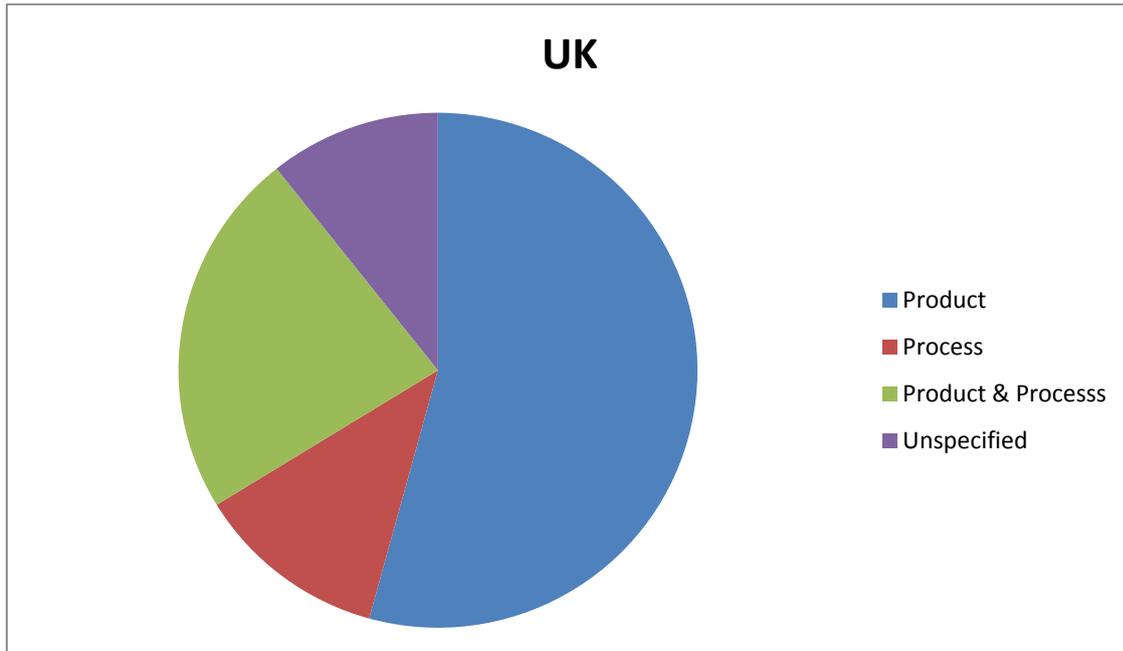


Figure 15: Patents held by UK holders, by type.

Of the 234 patents held by UK companies, 127 (54%) were for products, 28 (12%) for process, 54 (23%) for product and process, and 25 (11%) were unspecified.

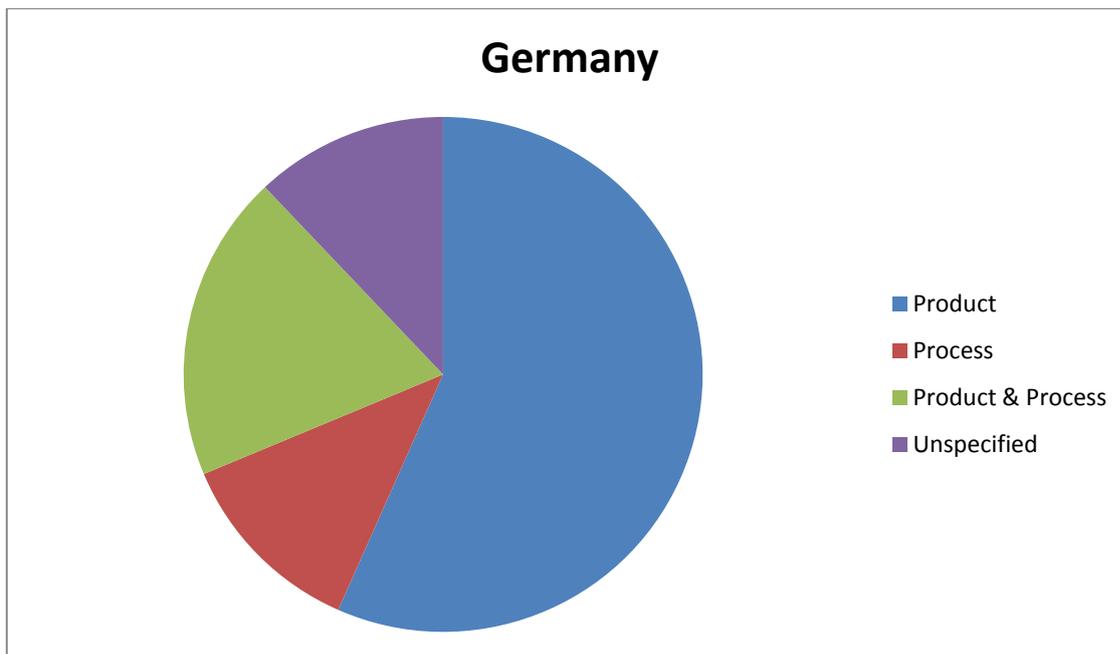


Figure 16: Patents held by German holders, by type.

Of the 166 patents held by German companies, 94 (57%) were for products, 20 (12%) for process, 32 were for product and process, and 20 (12%) were unspecified.

Patents held by South African companies

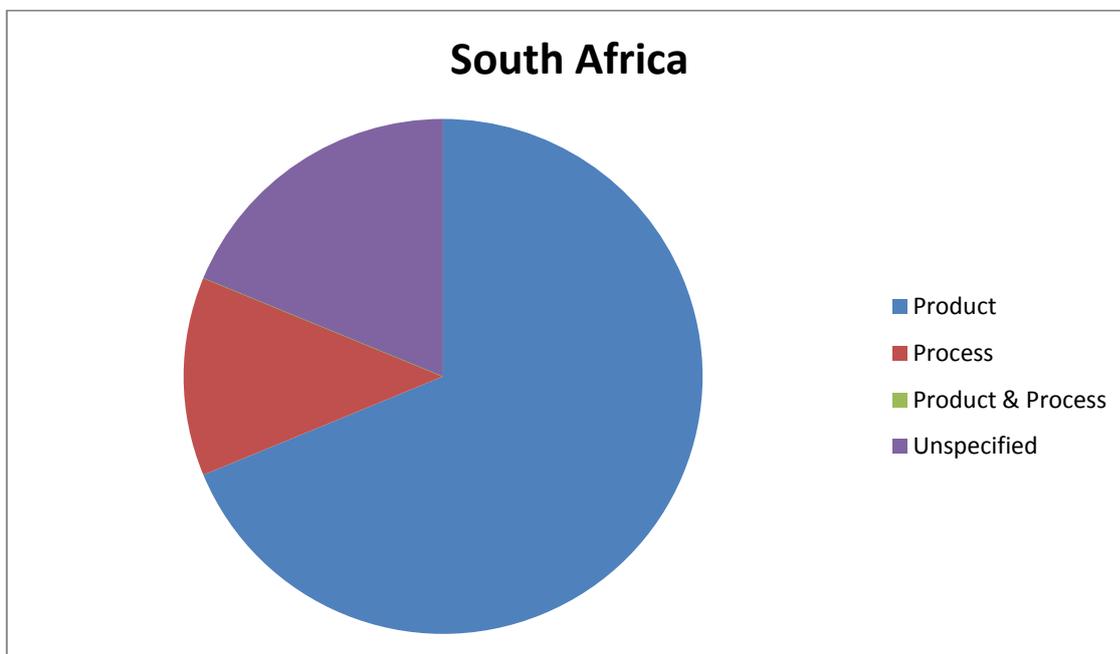


Figure 17: Patents held by South African holders, by type.

Of the patents held by South African companies, 8 (67%) were for products, 2 (17%) for process, and 2 (17%) were unspecified.

Patent No	Expiry	Title	Applicant	Ther Class	Type	INN
2005/07739	25.09.25	Novel composition relating to treatment of allergies	Pharmachoice Healthcare (Pty) Limited.	R	Prod	
2006/01622	11.12.27	Treatment preparation and method for cell-based myocardial regenerative therapy.	Bio Hrxt (Pty) Ltd.	C	Prod	
2006/03135	19.04.26	Skin burn treatment ointment	Irene Elizabeth Snyman	D	Prod	
2007/01036	17.07.25	Anti-histaminic composition	APL Cartons (Proprietary) Limited	R	Prod	
2007/04160	21.05.27	Treatment of parasitic infections in humans and animals	South African Medical Research Council; University of Cape Town	P	Process	
2006/09113	31.10.26	A method for detecting mycobacterial infection	University of Pretoria	J	-	
2007/01932	05.03.27	Pharmaceutical composition	Bayer Healthcare AG.	-	Prod	
2006/07508	07.09.26	Pharmaceutical composition	Gast, Kevin	-	Process	
2007/10786	12.12.27	Heterogeneously configured multiparticulate gastrointestinal drug delivery system.	University of the Witwatersrand. Johannesburg	-	Prod	
2007/06393	31.01.26	Method for determining	National Health Laboratory	J	-	

		HIV-1 viral load	Service, University of the Witwatersrand, Johannesburg.			
2007/01933	05.03.27	Pharmaceutical composition in the form of a water soluble solid dosage form	Bayer Healthcare AG	-	Prod	
2007/05708	10.07.27	A composition	Vermeuer. Willem Adriaan.	L	Prod	

Table C: Schedule of patents held by South African holders.

Distribution of patents by companies

The leading patent holders are listed below.

Company	Country	No of Patents	%age of total grant
AstraZeneca	UK	88	4
Novartis AG	Switzerland	49	2
Wyeth	US	43	2
F Hoffmann-La Roche AG	Switzerland	35	1
Pfizer Products Inc	US	32	1
Merck Patent GmbH	Germany	29	1
Various	South Africa	12	0.5

Table D: Schedule of leading holders of South African patents (2008).

7. 'Transparency' of patent system

Patent Registration procedure

The following figure illustrates the procedure followed in the grant of a patent.

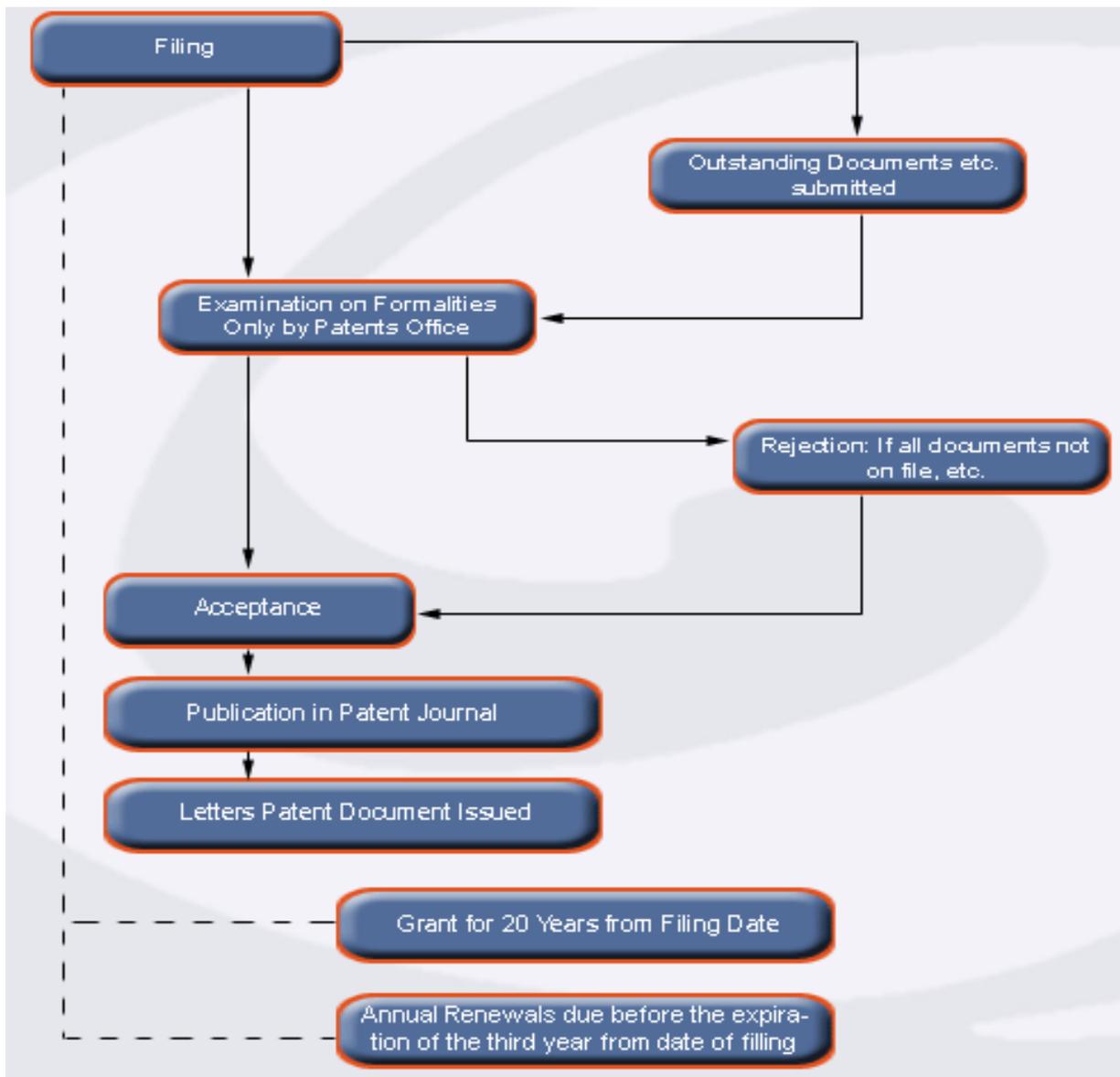


Figure 18: Procedure for patent grant (CIPRO
http://www.cipro.gov.za/products_services/patents_registration.asp.)

The South African equivalent of the patent office is the Companies and Intellectual Property Registration Office (CIPRO), a division within the Department of Trade and Industries. The Office specifies a three-step procedure for the registration of a patent, with a formal examination procedure usually taking up to six months from the lodgement of a complete application. Once the formalities have been complied with, the application is accepted and the applicant is required to publish the patent in the *Patents Journal* which, according to the CIPRO website ‘allows members of the public to lodge objections’ within three months. If there are no objections, the Patents Registrar will issue a Patent Certificate (Department of Trade and Industry). This information appears to be misleading as the Act makes no provision for opposition, and a patent is automatically sealed on acceptance by the Registrar (Burrell, 1999). In effect, CIPRO is a non-examining office, with applications being approved provided they comply with the formal requirements (Zdrakova, 2009). This is a major drawback as it has the potential to admit patents of low or inferior quality, meaning that they may not entirely satisfy the requirements of novelty, inventive step and industrial applicability, strictly applied.

8. Patent Litigation

A review of court proceedings revealed that only a small number of pharmaceutical patent challenges have been reported in the case law. These statistics are limited to matters which are brought to court, and do not include cases which might have been settled out of court.

Case No	Parties	Patent No	Patents/Products Involved	Outcome
2003 BIP 5	Glaxo Group Ltd v Cipla-Medpro (Pty) Ltd	92/9167	Aerosol formulation for use in medicaments by inhalation	Application granted to suspend an application for revocation of patent until pending application for amendment of patent decided.
2005 BIP 1	Pfizer Ltd & Another v Cipla Medpro (Pty) Ltd & Others	87/2439	NORVASCO (active ingredient besylate salt of amiodipine)	Application granted for order to (a) Correct certain clerical errors in the patent claims, and (b) Interdict respondents being generic producers of NORTWIL (having same active), from marketing same, pending revocation proceedings.
2007 BIP 59	Glaxo Group Ltd v Cipla Medpro (Pty) Ltd & Others	90/7136	Medicaments relating to treatment of asthma & other respiratory disorders	Application granted to strike out irregular opposition procedure to the patent holder’s application for amendment of patent, while revocation proceedings pending.

2007 BIP 66	Glaxo Group Ltd v Cipla Medpro (Pty) Ltd & Others	90/7136	Medicaments relating to treatment of asthma & other respiratory disorders	Respondent granted leave to intervene an application to amend the patent.
2007 BIP 91	Glaxo Group Ltd v Cipla Medpro (Pty) Ltd & Others	90/7136	Medicaments relating to treatment of asthma & other respiratory disorders	Application to amend the patent while revocation proceedings pending granted and respondent's application for postponement of the amendment application refused.
2008 BIP 79	H Lundbeck A/S & Another v Cipla Medpro (Pty) Ltd	89/4476	Escitalopram (marketed as CipraleX)	Application refused for (a) Correction of clerical errors in, amendment of, claims of patent and (b) Interdict to restrain generic producer of escitalopram from marketing same.
2008 BIP 107	H Lundbeck A/S & Another v Cipla Medpro (Pty) Ltd	89/4476	Escitalopram (marketed as CipraleX)	Application refused for (a) Amendment of patent, and (b) Temporary interdict restraining respondent from selling generic product Lexamil.

Table E: Schedule of South African patent litigation for period 2003-2008.

The following observations may be made from the foregoing data:

- In contrast to large number of pharmaceutical patents granted (more than 2400 for 2008 alone), the volume of litigation is minute.
- The fact that there is no patent examination system both results in an inordinately large number of 'weak' patents, as well as closes the opportunity for pre- and post-grant opposition proceedings.

- Thus patents are litigated primarily through applications to revoke, or where the holder alleges infringement.
- In the instances where revocation proceedings have been initiated on the basis that the patent is unclear and not obvious (Pfizer & Ano v Cipla Medpro & Ors 2005 BIP 1) the court refused to revoke, accepting that the besylate salt was itself unexpected, constituted an advance on the prior art, and represented an inventive step forward.
- Thus, despite the provisions of the Patents Act which set a high standard for patentability, the courts are applying a fairly low standard for patentability.

9. Conclusion

Health and medicines regime:

- Some 82% of the population is dependent on the public health system for access to health care.
- However, of the almost 9% of GDP spent on health in 2009, 5.2% was in the private sector (serving about 18% of the population) and 3.7% in the public sector (serving 82%).

Pharmaceutical market and production:

- South Africa has a highly developed pharmaceutical system, with considerable local capacity, some generic manufacturers having been in existence for over 100 years.
- But local research and development is restricted largely to formulation issues, with some new drug discovery projects in public-private partnerships and academic research centres.
- South African companies control 39% of the local market, with foreign companies predominating with 61%.
- The leading individual company is South African – Aspen Pharmacare – with 17% of market share.

Medicines regulation:

- The medicines regulator is the Medicines Control Council which assess medicines for registration in terms of the criteria of quality, efficacy and safety.
- The public health sector uses predominantly generic products, with some occasional branded medicines.
- There is a limited degree of price regulation, exercised by the Minister of Health, for the private sector.
- Since 2003, the requirement of the mandatory offer of generic substitution, in order to promote the use of cheaper generics, has been applied.

- Generics account for about 50% of the private sector share, by volume.

Intellectual property protection:

- The essential requirements for the grant of a patent are: novelty, inventive and industrial applicability.
- New uses and new forms are not patentable, once the substance forms part of the state of the art.
- But, as South Africa is a non-examining system, this (theoretical) high standard is not maintained.
- No opposition procedures are available.
- Some exceptions (early working) are available, but there is no research exception.
- There are substantial provisions for compulsory licences and government use orders, although these provisions have not been used in respect of a single pharmaceutical product.
- Parallel importation is permitted, the country subscribing to international exhaustion regime.
- There is a progressive competition law framework, and strong action has been taken against abusive and collusive practices against several, including pharmaceutical, companies. This area of law has proven to be the most effective legal remedy thus far for increasing access to medicines.
- Data for clinical trials enjoy protection from public disclosure, but are referenced for the approval of generic follow-ons.

Analysis of database:

- 58% of the patents were for products; 18% for products and processes; 10% for processes; and 14% were unspecified.
- The main therapeutic class comprising the patents were: Anti-neoplastic and immunomodulating agents (18%); Nervous system (13%); Anti-infectives for systemic use (13%); Alimentary tract and metabolism (7%); Cardio-vascular system (6%); Musculo-skeletal system (5%); Genito-urinary system and sex hormones (3%); Respiratory system (3%); Blood and blood-forming organs (3%); Dermatologicals (2%); Sensory organs (1%); Systemic hormonal preparations, excluding sex hormones and insulin, and anti-parasitics (1.5%); and unspecified by type were (24.5%).
- In terms of country of origin, the USA leads with (49%), followed by the UK (10%); Germany (7%); No country indicated (6%); France (4%); Japan (3%); Switzerland (3%); Sweden (3%); India (2%); Denmark (2%); Netherlands (1%); Italy (1%); South Africa (1%); China (0.5%); and Brazil (0.1%).

Transparency:

- South African does not have an examination system, but rather follows a formality-based approach.
- It takes between 6 months and 1 year to approve a patent.

Litigation:

- While a large number of patents is granted each year, the level of litigation is minute.
- This results in the granting of a large volume of 'weak' patents, as the courts have been applying a fairly low patentability standard, especially when it comes to new forms of existing compounds.

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