



Access to Medicines and Drug Regulation in Developing Countries: a Resource Guide for DFID

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1 INTRODUCTION - MEDICINES REGULATION IN DEVELOPING COUNTRIES – NECESSARY SAFEGUARD OR UNNECESSARY BARRIER?

The World Health Organization has popularised the approach that access to medicines, whether in developed or developing countries, is reliant on four interlocking factors: rational selection of the medicines to be used, affordable prices for those medicines, sustainable financing of healthcare (including medicines) and reliable health and supply systems. An effective medicines regulatory authority (MRA) is a crucial part of a “reliable health and supply system”.

Medicines registration is the process by which a national or regional MRA approves the use of a medicine in a particular country, having considered evidence of the medicine’s safety, quality and efficacy. It is thus primarily concerned with protecting public health. However, where medicines regulatory processes are unwieldy and delay entry of needed medicines in a particular market, they can be seen as a barrier to access as well as to profits and the growth of the pharmaceutical industry. Pre-marketing assessment of safety, quality and efficacy is however only one component of a medicines regulatory system. In addition, attention must be paid to ongoing assessment and inspection of the entire pharmaceutical supply chain (including manufacturers, importers, exporters, wholesalers, distributors and final sellers), maintenance of a register of approved products and post-marketing surveillance (including random quality checks and pharmacovigilance systems), control over the promotion and advertising of medicines and the provision of medicines information. Lastly, there is a view that issues related to the rational pricing of medicines and considerations of cost-effectiveness may also legitimately fall within the ambit of the medicines regulatory agency.

2 THE DEBATE

Developing countries face considerable challenges in ensuring greater access to medicines, yet also ensuring that the medicines that are available are safe, of acceptable quality and efficacious. While often under-resourced and poorly equipped to assess increasingly complex data, their MRAs are expected to register medicines more quickly and at the lowest possible cost. They must decide how to handle applications for new chemical entities (NCEs), interchangeable multi-source medicines (IMMs, also referred to as “generics”), new fixed-dose combination products (FDCs) and even traditional or complementary medicines. New chemical entities are novel molecules developed by researchers and subject to patent protection for a limited period of time. Once the patent expires (or a license is issued), copies of the medicine may legally be made. These are termed multi-source medicines and should in most cases be interchangeable with the original medicine. Regulators must also acquire the relevant technical expertise and organise their processes in order to facilitate the use of to use flexibilities in international trade agreements to improve access to medicines, such as compulsory licensing and parallel importation. The following are just some of the questions that have been raised. The emphasis is on issues related to improving access to essential medicines. Many other issues are also deserving of attention, but are beyond the scope of this exercise.

Other sites worth visiting include:

- The ELDIS Health Resource Guide on access to treatment, drug costs and traditional medicines (see <http://www.eldis.org/health/index.htm>) and the Eldis Health Systems Resource Guide on access to medicines and international issues (see <http://www.eldis.org/healthsystems/access/index.htm>).

2.1 Should developing country regulators build their own capacity or rely on regional efforts or even larger regulators in developed countries?

Developing country regulators are often under-resourced and lack access to the high levels of scientific expertise needed for the effective assessment of registration dossiers for new chemical entities (NCEs) and interchangeable multi-source medicines (IMMS, or 'generics'). It has been argued that:

- It is better for developing countries to rely on the assessments of major medicines regulatory authorities, such as those in the US and Europe, when faced with an application for registration of an NCE.
- Regional co-operation is needed when considering applications for IMMs, as the needed expertise is also in short supply.
- In specific areas, the WHO pre-qualification programme may assist developing countries.

2.2 How should medicines regulatory systems be funded and how should their performance be assessed?

Funding regulatory systems and retaining suitably qualified staff is a challenge in all settings. Where user fees are used to co-fund or entirely fund regulators, the time taken to complete the assessment of a registration dossier is often a key measure of its performance. It has been argued that:

- Governments should accept the responsibility for funding medicines regulation, in the interests of public safety and to avoid regulatory capture by fee payers.
- Although important to pharmaceutical manufacturers and patients, over-emphasis on the time taken to complete the registration process may detract from the quality of the process.

2.3 What impact would "harmonization" have on developing country regulators?

The International Conference on Harmonization (ICH) has sought to improve the efficiency of medicines registration in the US, Europe and Japan by creating common templates and standards. Regional harmonization has also been achieved in Europe, with procedures for reciprocal and mutual recognition of decisions. The WHO has also been active in setting standards at the international level. It has been argued that:

- Applying ICH standards and processes to non-ICH countries will increase costs and hamper access to necessary medicines, particularly IMMs.
- WHO is the more appropriate intergovernmental organization to set international standards.
- Regional efforts are difficult to arrange and may result in the domination of the area by the strongest regulator involved.

2.4 How do intellectual property rights and medicines regulation interface and affect access to medicines?

Completely different laws and regulatory authorities usually govern medicines regulatory issues and intellectual property rights. However, the extension of a single standard of intellectual property right protection to all inventions (including medicines) and its application to all countries that are signatories to the agreements that created the World Trade Organization (WTO) has created new barriers to access to essential medicines. These barriers have been recognised and their potential impact on public health acknowledged, and in response, important flexibilities in respect of the Agreement on Trade Related Intellectual Property Rights (TRIPS) can be exploited by developing countries. Two of these are compulsory licensing and parallel importation. However, it has been argued that:

- An effective national MRA must be in place to allow for the effective operation of compulsory licenses and parallel trade, since these two flexibilities must generally be utilised at the country-level.
- If health, patent and medicines regulatory authorities are not working closely together, the potential benefits of these flexibilities may not be realised.
- Many developing countries do not have the necessary legislation in place to allow for the best use of these flexibilities.
- Bilateral trade agreements pose a potential threat to such activities if they seek to impose “TRIPS-plus” conditions.

3 THE EVIDENCE BASE

3.1 Should developing country regulators build their own capacity or rely on regional efforts or even larger regulators in developed countries?

NCE dossiers are generally assessed by the US and European authorities. Their assessments could therefore be relied upon by developing countries as sufficient proof of safety, quality and efficacy. Applications for interchangeable multi-source medicines (IMMs) may be specific to developing countries, perhaps depending on local patent status and law or local manufacturers. However, they also demand expertise that is in short supply. Regional co-operation may allow scarce expertise to be more efficiently applied. However, inspection of manufacturing plants may still be necessary, especially if products are made only for export. A particular challenge is the consideration of applications to register fixed-dose combinations (FDCs). There have been keen debates on which types of data are needed for a particular combination. In some specific areas (HIV/AIDS, TB, malaria), the WHO pre-qualification project may be relied upon by countries without access to a competent MRA, but this needs to be clearly differentiated from the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce. One of the ways in which resources have been shared has been through the Pharmaceutical Inspection Convention and the Pharmaceutical Inspection Co-operation Scheme (PIC/S). Membership of the PIC/S is seen as evidence of an MRA being “stringent”. However, few developing country MRAs are members of the PIC/S.

Recommended reading ... See Section 4.2

3.2 How should medicines regulatory systems be funded and how should their performance be assessed?

The fees charged by medicines regulators vary considerably, but most developing country regulators are profoundly under-resourced. Where user fees have been linked to promises of completing assessment of the dossier in a particular time, this may increase pressure on regulators to approve new medicines without having access to all the necessary data. Patient demand may also contribute to this pressure. Reliance on user fees as a funding source may make regulators more likely to see pharmaceutical manufacturers as the constituency to which they are primarily responsible, rather than the public. This may also bias their views on the reliability of industry-supplied data. Other measures of performance, accountability and transparency have been developed, but are seldom applied.

Recommended reading ... see Section 4.3

3.3 What impact would “harmonization” have on developing country regulators?

The ICH process has made some useful contributions, such as the Common Technical Document (CTD) standard for trial reports. Using this format avoids the unnecessary costs of reformatting submissions for each country in which registration is sought. It is of greatest use when preparing NCE applications. However, a far greater problem is faced in harmonising requirements for IMM (generic) registration.

A WHO study of medicines regulation in 10 countries showed that generic requirements vary considerably. There are also considerable challenges facing smaller MRAs that lack the technical expertise necessary to decide when bioequivalence data are needed and how to assess such data when they are presented. It is important to note how long the EU process has taken to achieve a “harmonised” environment. Good evidence of the impact of applying ICH standards on medicines access in non-ICH countries is lacking.

Recommended reading ... See Section 4.4

3.4 How do intellectual property rights and medicines regulation interface and affect access to medicines?

It is important to stress that MRAs are not in the business of policing patents, nor should their decisions be influenced by consideration of the patent status of a product. This has been the case in many settings, for example where so-called “Bolar” exceptions are used to allow the submission of a dossier to the MRA prior to expiry of the patent on that particular product and/or process. Although the potential of the TRIPS “flexibilities” have been well described, there is little actual evidence of their use in the field. There are however, many ways in which a lack of co-ordinated action between health, patent and medicines regulatory authorities can delay access to a medicine that is the subject of a compulsory license, a parallel importation effort or which has to be imported into a non-producing country from a producing country. Of great concern is the trend for bilateral trade agreements between developed and developing countries to include additional intellectual property protection beyond the minima stipulated in the TRIPS Agreement. These include provisions for data protection for a number of years after submission to an MRA. In such cases, subsequent applications (for example for IMMs) cannot be considered on the basis of access to or even mere reliance upon the safety and efficacy data included in the initial submission. To repeat such studies would be not only wasteful and time-consuming but also potentially unethical. Finally, the impact of China and India becoming TRIPS compliant has yet to be felt.

Recommended reading ... See Section 4.5

4 RECOMMENDED READING

4.1 Introduction

- World Health Organization. The World Medicines Situation (2004).
http://www.who.int/medicines/organization/par/World_Medicines_Situation.pdf

This is a major new publication, which updates a 1988 edition (The World Drug Situation). It outlines the current situation in respect of world medicine production, research and development, international trade, sales and consumption, national medicines policies, access to medicines, rational use of medicines and medicines registration.

- WHO model web site for Drug Regulatory Authorities
<http://www.who.int/medicines/organization/qsm/activities/drugregul/dramodelweb.shtml#1>

This WHO site provides guidance to medicines regulatory authorities on the scope and content of their own web sites. It should contribute to making medicines regulatory information more widely available and accessible. It should also contribute to greater transparency of a process long considered “secret” in many countries.

4.2 Should developing country regulators build their own capacity or rely on regional efforts or even larger regulators in developed countries?

- World Health Organization. The World Medicines Situation (2004).
http://www.who.int/medicines/organization/par/World_Medicines_Situation.pdf

Chapter 9 of this report deals with medicines regulation. It also outlines the challenges facing developing country MRAs and lists the regional initiatives that are currently underway.

- Access to medicines in under-served countries: What are the implications of changes in intellectual property rights, trade and drug registration policy? DFID Health Systems Resource Centre (2004).
http://www.dfidhealthrc.org/shared/publications/Issues_papers/ATM/DFID_synthesis_aw.pdf

This is an overview paper of seven studies commissioned by the Access to Medicines team at the Department for International Development (DFID) and focused on issues of current concern and debate in developing countries.

- Hill S, Johnson K. Emerging challenges and opportunities in drug registration and regulation in developing countries. DFID Health Systems Resource Centre (2004).
http://www.dfidhealthrc.org/shared/publications/Issues_papers/ATM/Hill.pdf

One of seven DFID-commissioned studies, this paper describes current drug regulation and registration processes in selected countries in order to understand how they affect the quality and availability of medicines in developing countries, develops policy recommendations as to how systems can more efficiently allow appropriate quality drugs to market, and discusses emerging challenges and requirements posed by compulsory licensing, drugs for neglected diseases, anti-

retroviral and anti-tuberculosis drugs. It draws partly on a study of medicines regulation in 10 countries commissioned by the WHO.

- Ratanwijitrasin S, Wondemagegnehu E. Effective drug regulation: a multicountry study. World Health Organization (2002).
<http://www.who.int/medicines/library/gsm/eff-drug-reg/isbn9241562064.doc>

This is a synthesis of studies carried out in 10 countries (2 developed, 8 developing), from which much of the data for the DFID study (see 3 above) was drawn. It provides an overview of the development of drug regulation in these countries, the resources available, the strategies applied in drug regulation implementation, and an analysis of the strengths and weaknesses in drug regulation in these countries.

- Use of the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce WHO/DAP/94.21. World Health Organization (1994).
<http://www.who.int/medicines/library/dap/who-dap-94-21/who-dap-94-21.pdf>

This report highlights the limitations of the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce, set up in 1975. If used properly, it should allow developing countries to import pharmaceutical products with some degree of quality assurance. However, it only provides formal assurance about the registration status of the pharmaceutical products concerned. The report suggested that exporting countries should subject pharmaceutical products for export to the same standards of control applied to locally consumed products.

- WHO pre-qualification project
<http://mednet3.who.int/prequal/>

This site provides access to all of the relevant documents about the WHO pre-qualification programme, applied to HIV/AIDS products and manufacturers (on behalf of the United Nations partners, including WHO, UNICEF, UNAIDS and UNFP), tuberculosis products and manufacturers (on behalf of WHO, the Global Drug Facility (GDF), Stop TB partnership and the Green Light Committee (GLC)) and malaria products and manufacturers (on behalf of WHO, Roll Back Malaria and Malaria Directorate). Although not intended to replace MRAs' efforts, it does cover much of the same terrain: the assessment of product dossiers containing data and information as required in the guidelines, norms and standards of the WHO, for safety, quality and efficacy; the assessment of manufacturers for compliance with WHO Good Manufacturing Practices (GMP) and data verification; and the assessment of Contract Research Organizations (CROs) for compliance with Good Clinical Practices (GCP) and Good Laboratory Practices (GLP), and data verification.

- Scientific and Technical Principles for Fixed Dose Combination Drug Products
<http://www.globalhealth.gov/Final%20Draft%204-22.doc>

This document, though “not intended to be a therapeutic or regulatory guideline”, is expected to inform regulatory practice. It stemmed from a meeting held in Gaborone, Botswana, in April 2004, under the auspices of the Joint United Nations Programme on HIV/AIDS (UNAIDS), World Health Organization (WHO), Southern African Development Community (SADC) and the United States Department of Health and Human Services (HHS), which brought together international regulators to discuss principles for the assessment of ARV FDCs to be purchased by PEPFAR

(President's Emergency Plan for Aids Relief). A more detailed regulatory guidance document for FDCs is currently being finalised by the WHO.

- Pharmaceutical Inspection Convention and the Pharmaceutical Inspection Co-operation Scheme (PIC/S)
<http://www.picscheme.org/>

The objective of the PIC/S, as explained on the site, is: "to pursue and strengthen the cooperation established between the participating authorities in the field of inspection and related areas with a view to maintaining the mutual confidence and promoting quality assurance of inspections, to provide the framework for all necessary exchange of information and experience, to coordinate mutual training for inspectors and for other technical experts in related fields, to continue common efforts towards the improvement and harmonisation of technical standards and procedures regarding the inspection of the manufacture of medicinal products and the testing of medicinal products by official control laboratories, to continue common efforts for the development, harmonisation and maintenance of Good Manufacturing Practice (GMP), and to extend the cooperation to other competent authorities having the national arrangements necessary to apply equivalent standards and procedures with a view to contributing to global harmonisation.". Of the European transitional countries, the Czech Republic, Hungary, Romania, the Slovak Republic and Latvia have joined. Only Singapore and Malaysia represent the developing countries.

- Guimier J-M, Lee E, Grupper M. Processes and issues for improving access to medicines: the evidence base for domestic production and greater access to medicines. DFID Health Systems Resource Centre (2004).
http://www.dfidhealthrc.org/shared/publications/Issues_papers/ATM/Guimier.pdf

There are many parallels between the debate on local production and that of building an effective local MRA. In this paper, the point is made that "Drug regulatory authorities and quality assurance systems need to be reinforced to ensure that only quality drugs reach the end-user through distribution systems", as too often access to medicines has been access to poor quality medicines. For the purposes of this study "quality medicines" were defined as "those that meet internationally recognized standards". In turn, these were taken to include those approved by the WHO Pre-qualification Project, or those made in countries participating in either the Pharmaceutical Inspection Cooperation Scheme and/or the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use⁴. The point was made that "[c]urrently few, if any, domestically produced drugs within [sub-Saharan Africa] SSA meet these standards".

4.3 How should medicines regulatory systems be funded and how should their performance be assessed?

- Ratanwijitrasin S, Wondemagegnehu E. Effective drug regulation: a multicountry study. World Health Organization (2002).
<http://www.who.int/medicines/library/gsm/eff-drug-reg/isbn9241562064.doc>

This is a synthesis of studies carried out in 10 countries (2 developed, 8 developing). It shows the vast differences in funding and resources available, but also the considerable variation in the time taken to complete an average evaluation. The report includes an extensive listing of possible measures of performance, accountability and transparency, but shows how seldom these have been applied by the MRAs assessed.

- Kaplan W, Laing R. Paying for pharmaceutical registration in developing countries. *Health Policy and Planning*, 2003, 18:237–248.
(not available free, but consideration should be given to accessing a full text version, or at least placing the Medline abstract on the site – see PMID 12917265)

This paper examines how the fees charged by MRAs may be used as a policy instrument to speed up regulatory approval, to encourage retention of quality staff and to stimulate introduction of generics versus new chemical entities. Based on analyses of 34 countries, it shows that the cost recovery function of these registration fees is not often related to the true cost of the pharmaceutical regulatory process and that there is little relationship between registration fees and drug approval times in developing countries. It suggests that developing countries should require that registration fees be based on accurate accounting of the cost of services provided and that they could be increased without disincentive to the pharmaceutical industry.

- Hill S, Johnson K. Emerging challenges and opportunities in drug registration and regulation in developing countries. DFID Health Systems Resource Centre (2004).
http://www.dfidhealthrc.org/shared/publications/Issues_papers/ATM/Hill.pdf

This paper describes current drug regulation and registration processes in selected countries in order to understand how they affect the quality and availability of medicines in developing countries, develops policy recommendations as to how systems can more efficiently allow appropriate quality drugs to market, and discusses emerging challenges and requirements posed by compulsory licensing, drugs for neglected diseases, anti-retroviral and anti-tuberculosis drugs. It outlines the risk of “regulatory capture” when regulators are dependent on user fees for funding.

- Abraham J. The pharmaceutical industry as a political player. *Lancet*. 2002 Nov 9;360(9344):1498-502.
http://www.sciencedirect.com/science?_ob=MIimg&_imagekey=B6T1B-475R8RN-11-1&_cdi=4886&_orig=search&_coverDate=11%2F09%2F2002&_qd=1&_sk=996390655&_view=c&_wchp=dGLbVzb-zSkWW&_acct=C000058881&_version=1&_userid=3002350&_md5=fbc1c85b8cef08dd5abfdea5b0dc4478&_ie=f.pdf

(an alternative source might be found for PMID: 12433532, or the abstract included)

This paper argues that “[p]harmaceutical companies want the safety and efficacy standards of regulators to be high enough to avoid frequent drug disasters, which bring the industry into disrepute, but not so high that they threaten their commercial viability”. It lists various ways in which “regulatory capture” may occur, concluding that all countries should move towards the public rights of access to regulatory information that exist in the US, that MRAs should identify a few key tests for each new drug application, which their own scientists could undertake independently of the manufacturer, that the state should reassert some responsibility for funding regulatory review, and that expert advisers to MRAs should be required to suspend all conflicts of interest during their time in office.

4.4 What impact would “harmonization” have on developing country regulators?

- Hill S, Johnson K. Emerging challenges and opportunities in drug registration and regulation in developing countries. DFID Health Systems Resource Centre (2004).
http://www.dfidhealthrc.org/shared/publications/Issues_papers/ATM/Hill.pdf

This paper describes current drug regulation and registration processes in selected countries in order to understand how they affect the quality and availability of medicines in developing countries, develops policy recommendations as to how systems can more efficiently allow appropriate quality drugs to market, and discusses emerging challenges and requirements posed by compulsory licensing, drugs for neglected diseases, anti-retroviral and anti-tuberculosis drugs. It lists a variety of regional “harmonization” and co-operation processes being undertaken, but also shows how difficult it is to achieve the aims of these efforts.

- Musungu SF, Villaneuva S, Blasetti R. Utilizing TRIPS flexibilities for public health protection through South-South regional frameworks. South Centre (2004).
<http://www.southcentre.org/publications/flexibilities/flexibilities.pdf>

This study identified the following constraints facing developing countries that wish to use the TRIPS flexibilities: lack of technical expertise, insufficient technical and infrastructural capacities for medicines regulations, bilateral and other pressures not to use the TRIPS flexibilities for public health purposes and/or to adopt TRIPS-plus standards, difficulties in regulating anti-competitive practices and abuse of intellectual property rights and difficulties in accessing pricing and patent status information. It argues that many of these constraints can be addressed by adopting complimentary policy and legal measures at the regional level.

- The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)
http://www.ich.org/UrlGrpServer.jserv?@_ID=276&@_TEMPLATE=254

This site provides access to the ICH, which states as its purpose: “to make recommendations on ways to achieve greater harmonisation in the interpretation and application of technical guidelines and requirements for product registration in order to reduce or obviate the need to duplicate the testing carried out during the research and development of new medicines”. Its objective is “more economical use of human, animal and material resources, and the elimination of unnecessary delay in the global development and availability of new medicines whilst maintaining safeguards on quality, safety and efficacy, and regulatory obligations to protect public health”.

- The European Agency for the Evaluation of Medicinal Products (EMA)
<http://www.emea.eu.int/>

This site provides access to the European regional MRA and its vast resources.

- Trouiller P, Salmen R, Myhr K, Folb P, Weerasuriya K, Gray A. The globalization of regulatory requirements, and the development and availability of medicinal products in developing countries: quality, efficacy and safety issues. MSF/DND/Working Group: The Crisis of Neglected Diseases, Developing Treatments and Ensuring Access. New York, March, 2002.
<http://www.accessmed-msf.org/upload/ReportsandPublications/2092002171222/3-2.pdf>
(note - this link did not work when last I checked – perhaps a copy can be

obtained from the DNIDi or MSF offices – however, the conf report at http://www.dndi.org/pdf_files/NYconfreport.pdf does include the sentiments expressed)

This input paper for the Drugs for Neglected Diseases initiative tracked the development of international harmonization efforts, from which developing country MRAs were largely excluded. While it is true that people in the developing world have generally benefited from the drug-regulatory framework established by the developed world, over-ambitious standards, such as those set by the ICH, can become a challenge for public health in the developing world. These rules threaten local regulators' autonomy to make drug decisions appropriate to their populations. It can be argued that there should not be a globally uniform rules-based technical approach to drug quality, safety, and efficacy. Rather, these issues should be tied to country-specific public health needs, but this requires that considerable support be given to MRAs in the developing world. In contrast, the WHO World Medicines Situation lists 4 positive reasons for global harmonizations: "in theory, only one set of guidelines need be set for all regions, and consequently the amount of duplicative human and animal experimentation is reduced"; "there can be cross-country exchange of expertise with minimum duplication of effort"; "improved and coordinated technical harmonization will give developing country DRAs greater bargaining/negotiating power when dealing with outside DRAs, multinationals and/or foreign manufacturers"; and "the cost of development of new drugs can be reduced, which ought to lead to lower prices; local products are more likely to be acceptable for export to other countries".

- World Health Organization. The World Medicines Situation (2004). http://www.who.int/medicines/organization/par/World_Medicines_Situation.pdf

Chapter 9 of this report deals with medicines regulation. Section 9.5 deals with international harmonization.

- World Health Organization. The Impact of Implementation of ICH Guidelines in Non-ICH Countries Report of a WHO Meeting, Geneva, 13-15 September 2001. <http://www.who.int/medicines/library/qsm/who-edm-qsm-2002-3/who-edm-qsm-2002-3.pdf>

This report highlighted the concerns around the application of ICH standards in non-ICH countries, particularly in the developing world. It noted the ways in which ICH standards were beginning to impact on non-NCE areas, notably on the registration of IMMs (generics). It called for greater WHO efforts in developing appropriate international standards, in consultation with the affected parties.

- World Health Organization. Marketing authorization of pharmaceutical products with special reference to multisource (generic) products: A manual for regulatory authorities. <http://www.who.int/medicines/library/qsm/manual-on-marketing/who-dmp-rgs-985.doc>

This is an example of a WHO standard, with particular emphasis on the registration of IMMs. It provides extensive guidance on all aspects of the registration process, including model forms and guidelines on national legislation.

4.5 How do intellectual property rights and medicines regulation interface and affect access to medicines?

- Baker B. Processes and issues for improving access to medicines: willingness and ability to utilise TRIPS flexibilities in non-producing countries. DFID Health Systems Resource Centre (2004).
http://www.dfidhealthrc.org/shared/publications/Issues_papers/ATM/Baker.pdf

TRIPS, the Doha Declaration, and the 30 August 2003 Decision enable countries with public health needs and with insufficient capacity to manufacture a needed medicine to import lower-cost products from other countries. This paper addresses varied ways by which a non-producing country may lawfully utilise TRIPS flexibilities, and looks at the internal and external forces which negatively affect non-producing countries' ability and willingness to use TRIPS-compliant flexibilities. Specifically, it demonstrates how unco-ordinated action between patent authorities and the MRA can delay access and nullify the benefits of the TRIPS flexibilities. This is a wide topic on which a lot has been written. However, this report provides a very practical guide, especially in respect of the complexities of using the August 2003 Decision to overcome the problems of non-producing countries.

- Hill S, Johnson K. Emerging challenges and opportunities in drug registration and regulation in developing countries. DFID Health Systems Resource Centre (2004).
http://www.dfidhealthrc.org/shared/publications/Issues_papers/ATM/Hill.pdf

This paper describes current drug regulation and registration processes in selected countries in order to understand how they affect the quality and availability of medicines in developing countries, develops policy recommendations as to how systems can more efficiently allow appropriate quality drugs to market, and discusses emerging challenges and requirements posed by compulsory licensing, drugs for neglected diseases, anti-retroviral and anti-tuberculosis drugs. In particular it outlines how the need for quick action in the case of compulsory licensing and parallel importation. It also explains the potential impact of extending data exclusivity, as is being asked for in many bilateral trade agreements currently under negotiation. If developing countries concede to these demands they may find themselves unable to approve new IMMs. An alternative is offered – reliance on published trial data – but the potential shortcomings of that approach are also noted.

- Correa C. Implementation of the WTO General Council Decision on Paragraph 6 of the DOHA Declaration on the Trips Agreement and Public Health. World Health Organization (2004).
http://www.who.int/medicines/organization/ood/WTO_DOHA_DecisionPara6final.pdf

The Doha Declaration (2001) recognised, in paragraph 6, that countries lacking or with insufficient manufacturing capacities in pharmaceuticals would not be able to effectively use compulsory licensing. This report indicates how the 30 August 2003 Decision can be used to overcome these problems.

- Correa C. Implications of the Doha Declaration on the TRIPS Agreement and Public Health. World Health Organization (2002).
<http://www.who.int/medicines/library/par/who-edm-par-2002-3/doha-implications.pdf>

This report outlines how the Doha Declaration can be used to improve access to medicines, by implementing the features that recognise the primacy of health concerns over those of profit. It characterises the Doha Declaration as “a strong

political statement that can make it easier for developing countries to adopt measures necessary to ensure access to health care without the fear of being dragged into a legal battle”.

- Drahos P, Henry D. The free trade agreement between Australia and the United States. *BMJ* 2004; 328:1271-2.
<http://bmj.bmjournals.com/cgi/reprint/328/7451/1271>

This short editorial outlines the potential impact of the US-Australia Free Trade Agreement, particularly changes to the ways medicines are selected for reimbursement in Australia and how data exclusivity may delay generic entry. The authors conclude that “The bilateral trade agreements now being negotiated by the United States seem to be designed to undermine the Doha agreement and promote a particular business model for the production of medicines that is based on ever stronger patent protection”. A more extensive argument is presented in Harvey KJ, Faunce TA, Lokuge B, Drahos P. Will the Australia-United States Free Trade Agreement undermine the Pharmaceutical Benefits Scheme? *Med J Aust.* 2004 Sep 6; 181(5): 256-9 (see http://www.mja.com.au/public/rop/ausfta/har10408_fm.pdf). The authors suggest that “the capacity of generic manufacturers to rapidly “springboard” their cheaper products from existing data on the expiry of a patent be unequivocally protected”.

- Lewis-Lettington R, Munyi P. Willingness and ability to use TRIPS flexibilities: Kenya case study.
http://www.dfidhealthrc.org/shared/publications/Issues_papers/ATM/Lettington2.pdf
- Lewis-Lettington R, Banda C. A survey of policy and practice on the use of access to medicines-related TRIPS flexibilities in Malawi
http://www.dfidhealthrc.org/shared/publications/Issues_papers/ATM/Lettington.pdf

These two country case studies describe the current context relating to access to medicines in Kenya and Malawi. Kenya currently obtains medicines from domestic and international sources. Local generic manufacturers play an important role, primarily for the public and not-for-profit sectors, but face significant hurdles. Critically, Kenya’s ability to maximise the benefits of its relatively advanced legislation to promote access to medicines is limited. Strengthening implementation efforts in various administrative authorities could however contribute to progress in this area. Malawi is more typical of non-producing countries, but needs considerable technical assistance if the current political will to engage with access to medicines-related and broader TRIPs-related initiatives is to be capitalised upon.

- Grace C, 2004. The effect of changing intellectual property on pharmaceutical industry prospects in India and China: considerations for access to medicines, DFID HSRC.
www.dfidhealthrc.org/Shared/publications/Issues_papers/ATM/Grace2.pdf

Sections 9 and 10 of this study show the way in which the transaction system for drug registration is thought to be skewed in favour of domestic companies, not least because of the conflict of interest that arises because the drug registration authority is charged with both drug approval and promotion of the domestic industry. The study concludes that despite the fact that China started respecting pharmaceutical product patents more than two years ago, the regulatory and legal infrastructure to support

IPR lags behind. The implication is that the introduction of a product patent system, when not accompanied by an institutional environment that supports IPR, may make the intended gains from compliance with TRIPS illusory in the short to medium term, whilst the welfare losses from reduced access to certain medicines may be more immediate and obvious. A second implication is that a multitude of country-specific institutions and processes - most notably in this case, the drug regulatory process - influence the practical impact from compliance with TRIPS, therefore we are likely to see some very different experiences and impacts as countries implement pharmaceutical product patent protection.