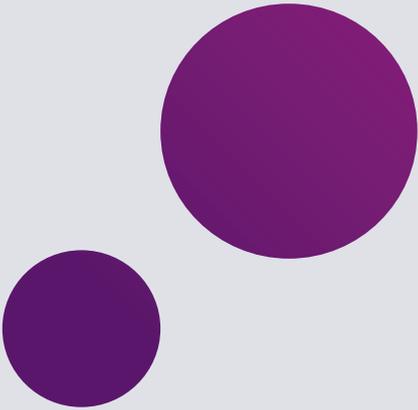




HEALTH ▸ HYGIENE ▸ HOME



COMMISSIONED BY:
RB in association with Proprietary Association of Great Britain



Consumer health: time for a regulatory re-think?

WRITTEN BY:



Foreword



JOHN SMITH / Chief Executive
Proprietary Association of Great Britain (PAGB)

Healthcare systems across the world are facing increasing pressures from growing and ageing populations. People are living longer but are not necessarily spending those extra years in good health. Rates of chronic illnesses such as heart disease, diabetes and COPD (chronic obstructive pulmonary disease) are growing and people are more dependent on support from healthcare professionals.

This presents a significant challenge, but by equipping more people with the skills to take responsibility for their own health and wellbeing, healthcare systems can free up resources and capacity to support those people living with complex chronic conditions.

In the UK alone we know there are 57 million General Practitioner (GP) appointments and 3.7 million visits to hospital accident and emergency departments for self treatable conditions. If all of those people were to practice self-care, with the advice of a pharmacist if needed, it could save the National Health Service £2.3 billion.

Improving health literacy among the general public, giving them accessible information and ensuring the system accurately signposts them to an appropriate service for their needs are central to empowering more people to self-care, but as this report suggests, the regulatory system has an important role to play in ensuring safe and effective medicines are available and accessible.

PAGB would like to see a more people-centric approach to regulatory decision making, which we believe will support self-care in practice. Over-the-counter (OTC) medicines are by nature different to prescription medicines, yet regulatory frameworks do not reflect this.

We believe that real world data which shows how people use, understand and interact with non-prescription medicines should be given an equal weighting to clinical trial data in OTC regulatory decisions.

To fully embed self-care behaviour, people must have easy access to a range of over-the-counter products with which to self treat their symptoms. Much more could be done to support the reclassification of medicines and provide people with more choice. Despite the significant investment required to switch a product from a prescription-only to non-prescription status, companies are granted only a very limited period of market exclusivity, which can act as a disincentive to innovation. Other issues discussed in this report, such as naming and umbrella branding, also limit consumer healthcare companies' ability to innovate in this market.

PAGB welcomes this report from The Economist Intelligence Unit and RB. I hope it will stimulate discussion on these very important issues.

A handwritten signature in black ink, appearing to be 'John Smith', written in a cursive style.

JOHN SMITH / Chief Executive, PAGB

Consumer health: time for a regulatory re-think?

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About this report

Consumer health: time for a regulatory re-think? is a report by RB in association with PAGB, written by the Economist Intelligence Unit. It looks at the changing healthcare environment and the role self-care plays and efforts at regulatory harmonisation, the barriers they have encountered, and prospects for the future.

The report draws on substantial desk research and in-depth interviews with 15 experts from industry bodies, regulators, academia and patient groups. Our thanks are due to the following experts for their time and insight during the in-depth interviews (listed alphabetically):

- ◀ Dr Vincent Ahonkhai, senior adviser, Global Health Regulatory Affairs, Bill and Melinda Gates Foundation
- ◀ Dr Sarah Branch, deputy director, Vigilance and Risk Management of Medicines Division, UK Medicines and Healthcare products Regulatory Agency (MHRA)
- ◀ Dr Hubertus Cranz, director-general, Association of the European Self-Medication Industry (AESGP)
- ◀ Helen Darracott, deputy chief executive, Proprietary Association of Great Britain (PAGB)
- ◀ Dr James Fitzgerald, director of health systems and services, Pan American Health Organisation (PAHO)
- ◀ Kaisa Immonen-Charalambous, senior policy adviser, European Patients' Forum
- ◀ Simon Pettman, executive director, International Alliance of Dietary/Food Supplement Associations (IADSA)
- ◀ Dato' Eisah Binti A. Rahman, senior director of pharmaceutical services, Malaysian Ministry of Health
- ◀ Dr Pathom Sawanpanyalert, deputy secretary-general, Food and Drug Administration Thailand
- ◀ Professor R. William Soller, editor-in-chief, *SelfCare* (an academic journal)
- ◀ David Spangler, senior vice-president, Consumer Healthcare Products Association (CHPA)
- ◀ Professor Thomas Szucs, head of medical economics, Institute of Social and Preventive Medicine, University of Zurich
- ◀ Michael Thomas, global partner, A.T. Kearney
- ◀ Andy Tisman, senior principal, IMS Health
- ◀ Malinee Uditananda, chair, Asia-Pacific Self-Medication Industry (APSMI)

The report was written by Dr Paul Kielstra and edited by Martin Koehring of the EIU.

May 2016

Executive summary

Non-prescription, or over-the-counter (OTC), drugs are an essential part of the most widespread element of healthcare provision: self-care. Their use is substantial, as reflected in the size of the market for them: US\$111bn in 2014 worldwide, or about 11% of all pharmaceutical sales. Moreover, volume and income from sales are increasing steadily as the market has been growing particularly in emerging markets.

This greater use of OTC pharmaceuticals is consistent with the policy of many governments to increase the role of patients in their own health, improve access to medications where consistent with safety, and to reduce costs to health systems.

This study looks at an important impediment to continued growth of the sector: an inconsistent regulatory environment. Although different aspects of the issue have been addressed at multilateral and regional levels, progress has been limited and slow – despite the possible benefits to health and economic outcomes a more coherent market could bring.

Drawing on substantial desk research and in-depth interviews with 15 experts from industry bodies, regulators, academia and patient groups, this study looks at efforts at regulatory harmonisation, the barriers they have encountered, and prospects for the future. Its key findings include:

Non-prescription drugs face regulation across a wide range of areas, in many of which the costs and benefits remain poorly understood.

These include constraints typical of the pharmaceutical industry more generally, such as data requirements and drug safety. They also encompass regulation shaping the ways consumers can purchase products, such as classification of the drug itself as OTC, the claims sellers may make, the sales channels through which the products can be sold, and whether a pharmacist needs to be involved in the transaction. Given the extent of this regulation, it is striking how little research is available on the impact that different forms of regulation have on access, pricing and usage of non-prescription drugs.

Regulatory regimes are highly inconsistent between countries, but research on the impact of the resultant market fragmentation is lacking. In some developing states in particular most drugs are – for all intents and purposes – available to anyone willing to pay, while sellers can make any claims they wish. In others, restrictions are much greater. This type of difference often results from the relative strength of regulatory bodies. Even in states with similar levels of economic development, however, extensive variation exists. For example, in Europe the type of sales outlet at which one can buy non-prescription drugs and the need for a pharmacist to be present at the transaction differ markedly by country. The common – and logical – assumption of experts interviewed for this study is that the resultant market fragmentation likely increases costs and impedes patient access to some degree; however, solid research on the extent of these costs is lacking.

Regulatory harmonisation efforts have tended to be tangentially and partially relevant for non-prescription pharmaceuticals rather than directly focused on them. This study examines a variety of regulatory harmonisation efforts often dating two decades. None has been directed specifically at regulation around OTC drugs as a whole. Instead, they have arisen either as efforts to reduce inconsistencies facing the pharmaceutical industry in general – usually with the broader aim of improving access – or as parts of efforts to remove barriers between countries in regional free trade agreements. In practice, both types of initiatives have tended to focus largely on areas amenable to scientifically objective criteria, such as efficacy, quality, and safety, rather than the wider range of regulatory fields affecting non-prescription drugs.

Effective harmonisation requires a holistic approach, a similar level of regulatory capacity and an understanding of the role of professionals and patients in care. An overview of efforts at regional regulatory harmonisation in different regions shows a number of common difficulties. Partial harmonisation can help reduce some regulatory burdens, but inconsistencies in one area often leak back into areas where rules ostensibly have been aligned. Hence, a holistic approach is required. Another issue is understanding how regulators in different countries work and, once accomplished, raising the capacity of weaker ones. Finally, the regulatory differences between countries often reflect deep-seated and divergent views of national medical authorities on the correct role of professionals and patients in care – and even cultural differences over what substances are effective. Different cultures take different views of the same issue, and these differences are reflected in varying regulations. These differences are normal and have to be respected; hence, overcoming them is not straightforward despite the benefits of harmonisation in terms of reducing costs and improving patient access.

There is little interest in greater regulatory harmonisation in this area probably because there is little agreement on what harmonisation should mean. Many experts interviewed for this study indicated that, while greater harmonisation of OTC regulation might be beneficial, none of the major relevant stakeholders were strongly pushing for wide-ranging change. Political and cultural differences impede progress, so that there is no agreement over the direction towards common regulation. As Dr James Fitzgerald of the Pan American Health Organisation puts it: “are you harmonising from the perspective of more rigorous regulations and control or toward freer access with greater self-care responsibility for the patient? There is no overall common understanding of what harmonisation should look like.” Moreover, harmonisation may be counterproductive if it does not improve patients’ ability to self-medicate effectively, as the example of the patient information leaflet (PIL) in the EU shows.

RB viewpoint

Empowering Consumers to Live Healthier Lives: Recognising the Vital Role of Self-Care



RAKESH KAPOOR / CEO RB



ZEPHANIE JORDAN / Vice President, Global Regulatory Affairs RB

When a challenge presents itself the answer is often staring you in the face. It is impossible to ignore the ever increasing and wide-ranging pressure on health systems, and continuing on the same trajectory is entirely unsustainable.

What is not fully appreciated however, are the levers that we already have at our disposal that can alleviate the pressure, one of which is self-care. A fundamental question we are facing is simply, whether self-care can reduce the global health burden and if so how? There is an overwhelming consensus that self-care can be immensely beneficial for the health, wealth and prosperity of individuals, communities and nations. For many, consumer health is the first and sometimes only choice in healthcare. For others the possibilities are wider, but as a whole the population is evolving. We are growing in numbers, our middle classes are expanding and we are living longer, all of which lead to increasing healthcare needs. In parallel, people's healthcare needs are changing. We are leading faster, busier lives, we are becoming more health conscious and proactive in the management of our health, and we are looking to access healthcare in a more modern way that fits with our lifestyle. The 'virtualisation' of healthcare is erasing traditional means of support and people want a more accessible and convenient model that better reflects other aspects of their fast-paced, digital life. Given the backdrop of spiralling healthcare costs and stretched resources, and to meet the demands of a changing world, what a nation can least afford is to ignore or be narrow in thinking about how to adapt to these changing needs. One question to answer is how can we better acknowledge the role of self-care?

What is self-care?

Self-care is defined, by the Self-Care Forum, as a lifelong habit for patients and the public dealing appropriately, effectively and safely with their own minor ailments and long term conditions, taking preventative measures to stay fit, and maintaining good physical and mental health and wellbeing. The term encapsulates consumer health and self-medication with over-the-counter or non-prescription medicines.

Self-care including maintaining good health, disease prevention, self-diagnosis and self-medication for symptomatic and disease management, brings social and economic benefits. Economic studies evaluating the value of self-care and over-the-counter medicines have shown that giving people the tools to responsibly self-care, results in reduced needless costs to society, health systems, individuals and companies. According to the AESGP, the social value of self-medication is realised by managing common health problems from home without necessarily involving the healthcare systems. As a result, valuable medical resources can be redirected to more serious illness. An AESGP study looked at the economic and public health value of self-medication and demonstrated the economic value of self-medication and the incremental benefits of an increase in the levels of

self-medication using a conservative 5% substitution rate (from professional care to self-care).¹ It is estimated that the total annual savings in the enlarged European Union (2004) from the shift of care to self-medication by 5% would exceed €16 billion.¹ In the United States OTC medicines create \$102 billion USD in annual savings relative to alternatives (doctor visits, diagnostic tests, and prescribed medication).¹ In addition to the economic benefits, self-care is what people *want* and it represents high consumer satisfaction associated with different aspects including convenience, avoiding embarrassment and immediacy of access.

This report looks in detail at the complex and varied regulatory environment for over-the-counter medicines and its role in access to self-care. It is reasonable to expect that within well defined guardrails, there is an opportunity to examine how a tailored regulatory approach including greater harmonisation or recognition of decisions of other jurisdictions and pursuing minimum effective regulation that balances benefits and risks of non-prescription medicines, can drive innovation and access to self-care while protecting people's safety. RB supports regulatory harmonisation that strikes a balance between the appropriate level of patient empowerment, and protecting patients and minimising risks. However, until advancing self-care is strongly advocated for in national and international health and medicines policy, any efforts at harmonising regulations is at risk of driving up barriers and potentially having the opposite effect.

“RB supports regulatory harmonisation that strikes a balance between the appropriate level of patient empowerment, and protecting patients and minimising risks.”

Numerous governments have set out specific goals to promote positive behaviour change and support and empower people to take more responsibility for their health and wellness, but the implementation of such policies has been significantly lacking or incredibly slow moving. As described in this report for example, a plan set out in NHS England's Five-Year Forward View, describes a focus on prevention and wellbeing and the importance of a self-care strategy. However, strides towards the development of policy and coordinated strategies to enable the goals of the Five Year Forward View have been slow to materialise.² In the US the FDA Non-prescription Safe Use Regulatory Expansion (NSURE) program could allow the use of innovative technologies to help educate consumers about issues related to novel switch programs. The aim is to enable appropriate and safe use of medicines 'switched' from prescription to OTC, although the agency said it will likely be several years before it is in place. A more cohesive, integrated and effective regulatory environment requires mobilisation of national and international stakeholders to advance the dialogue and engage in coordinated effort to break down unnecessary health barriers.

Implementation of self-care policy has not been prioritised by governments and many continue to take a paternalistic approach to the health of their citizens. OTC medicines play an increasingly vital role in the wider healthcare system but one of the challenges here is that their role and the role of self-care is not clearly defined or recognised by decision makers.

The lack of clarity and appreciation of self-care and self-medication presents a barrier to progress and until government administrators have a mandate to implement and there is a platform and willingness to drive the discussion, the status quo is likely to continue.

In terms of harmonisation of the regulatory environment, ultimately the goal should be to look for reasons to approve products, not to block them. One of the many challenges that regulation for non-prescription medicines faces is the fact that the framework for reviewing OTC products is based on prescription medicines. Non-prescription medicines by their very nature should be approached in a different way. The system to regulate consumer health products needs to be fit for its purpose and that means it needs to differ from the system to regulate prescription products. A balanced benefit risk evaluation for Marketing Authorisations is essential for the full potential of self-care to be reached. This means accepting that non-prescription medicines do not enjoy patent protection and by their nature have their safety and efficacy established by scientific studies that were not conducted to today's standards but for the most part have been verified by many years of safe and effective use in the real world. To impose today's standards for new chemical entities onto non-prescription medicines is not necessary or consistent with a philosophy to find reasons to approve or expand access to medicines for self-care.

Companies including RB invest substantial effort, resource and expertise in product development, switches or reclassifications, to enable suitable products to be made available to people over-the-counter. However, currently there are limited incentives in the form of market exclusivity or data protection following switches to encourage companies to pursue innovative approaches or switch which in turn contribute to the desired self-care paradigm with invested and responsible people at the forefront.

The World Self-Medication Industry (WSMI) echoes this and while recognising that regulatory environments differ, encourages systems that include an appropriate period of data protection in order to encourage innovation in new self-medication treatments.³

In addition to this and as highlighted by the PAGB, there is a need for a people-centred approach to OTC regulation. The current regulations with regards to packaging and patient information are designed with healthcare professionals in mind rather than in a way that empowers consumers with information to make informed decisions about their own health and which medicine to use. Better education and awareness is vital and of course the role of the pharmacist is pivotal. Pharmacists are the gateway to an effective system, and appropriate education, training and resources are required for a more collaborative approach to health. **▶**

The creation of a more open market through measures such as competitive pricing, appropriate umbrella branding, trade agreements, harmonisation efforts and recognition of regulatory decisions in other countries can promote self-care while protecting patient safety. Inequalities between countries in access to non-prescription medicines can be reduced. Behaviour change can be supported and encouraged. A truly holistic approach is needed to make the difference towards health and wellness empowerment and greater independence.

“RB’s vision is a world where people are healthier and live better. We believe it’s our responsibility to drive discussion on this topic and foster change.”

RB’s vision is a world where people are healthier and live better. We believe it’s our responsibility to drive discussion on this topic and foster change. Until self-care is taken seriously at a national and international health and medicines policy level it will be difficult to break down many of the barriers to make self-care more accessible. We echo and applaud many of the findings of this report and want to kick start the international conversation with regulators and other stakeholders to evolve the policy position and subsequent regulatory framework to foster self-care as one way to reduce pressure on health systems and advance consumer engagement in managing their own health. We challenge all stakeholders to look outwardly and take action to improve the appreciation of the specific role of self-care and non-prescription medicines, and begin a deeper dialogue about issues that will ultimately improve lives and save money.

A call for action

RB seeks to support people all over the world to have improved access to consumer health and we believe that changes in regulation must be built on a foundation of evidence and deep consumer insights. Besides providing innovative self-care medicines and solutions, the industry must also take on the greater challenge of educating and supporting the public to effectively self-care in an increasingly information rich and digitally connected world.

Some of the challenges described in this report make change difficult however and we cannot foster change alone. We need a higher level mandate to improve policy on an international scale to really make a difference. The mission of the World Health Organization (WHO) is to provide global leadership in public health and we urge WHO to work in partnership with stakeholders to facilitate a change in the form of a set of WHO Guiding Principles to which governments, industry, regulatory bodies and healthcare system decision makers can adhere to encourage self-care and make self-care more accessible to more people. We also urge progressive nations to accelerate and lead this change.

Guiding principles:

- ◀ Call for governments to acknowledge and effectively build self-care into national health policy
- ◀ Establish a defined role for self-care which will provide a platform to drive the discussion on change
- ◀ Agree to the objective of designing the minimum necessary regulation to promote self-care while protecting patient safety
- ◀ Create a specialised regulatory approach designed to encourage mutual recognition, help less developed regulatory systems to improve capacities, and genuinely encourage enhanced consumer empowerment

See report conclusion – prospects for change...p29

Non-prescription medicines: where self-care and regulation collide

Healthcare costs are rising globally as the world's population continues to expand – set to grow by more than 2bn to almost 10bn by 2050 – at the same time as population ageing accelerates, with life expectancy at birth rising from around 70 to 77 during that period, according to UN projections.⁴

More and more people will be affected by a rise in chronic diseases. The Economist Intelligence Unit expects global healthcare spending to increase by around 4.3% a year on average over the next five years, to just over US\$9trn by 2019.

This puts pressures on squeezed healthcare budgets in developed countries and is set to cause challenges for emerging economies too. Hence, a new paradigm in healthcare is emerging: value-based healthcare, which looks at health outcomes of treatment relative to cost, “driven by the widespread recognition that historical trends in costs of healthcare are unsustainable in developed economies and are what emerging economies can ill afford to replicate.”⁵

The rise of patient empowerment and self-care

Against this backdrop, healthcare systems are looking for savings across the system and across types of disease – from minor illnesses to life-threatening diseases. For most healthcare systems the rise in chronic, non-communicable diseases is the priority. However, governments are also looking at strengthening education, prevention and empowering patients to take charge of their own health. Various studies have found that anywhere between two-thirds and over 90% of medical symptoms that people experience in developed countries with good medical access are dealt with entirely by patients.⁶ The round figure made conventional wisdom through frequent repetition is 80%.

Some countries are actively promoting a self-care agenda. For example, NHS England's *Five Year Forward View* of October 2014 devoted a whole chapter to empowering patients and engaging communities.⁷ At the Annual Self-Care Conference in London in November 2014, Earl Howe, then Parliamentary Under Secretary of State for Quality at the Department for Health, mentioned two important reasons for NHS England embracing a self-care agenda. First, it makes financial sense: he says the self-care agenda is key “if the NHS is to remain sustainable.” Second, he explains that “it is what we know patients want to do.”⁸

Individuals looking to self-treat have a range of options, such as changing diet or lifestyle, or using healthcare apps, as patients become better informed and knowledgeable about their own health. Some of the most powerful weapons in the self-care armamentarium, however, come directly from medical science: non-prescription or over-the-counter (OTC) pharmaceuticals. This report will focus on this latter area.

The size and growth of the OTC market indicates the substantial and increasing extent of their use. Even though they tend to be low-cost products, worldwide sales of these drugs reached US\$111bn in 2014, according to IMS, a healthcare consultancy. This represents just under 11% of the entire pharmaceutical market. **▶**

“Some of the most powerful weapons in the self-care armamentarium, however, come directly from medical science: non-prescription or over-the-counter (OTC) pharmaceuticals”

Data compiled by IMS Health for the Proprietary Association of Great Britain (PAGB), the trade association representing manufacturers of branded OTC medicines, self-care medical devices and food supplements, show that **minor ailments in General Practice cost the NHS around:**

£2bn (US\$3.1bn) in 2006–7 or...

2.7% of the total NHS budget of...

£75bn during that financial year.

Of this, the top 10 minor ailments (see Figure 1) were responsible for



of consultation costs



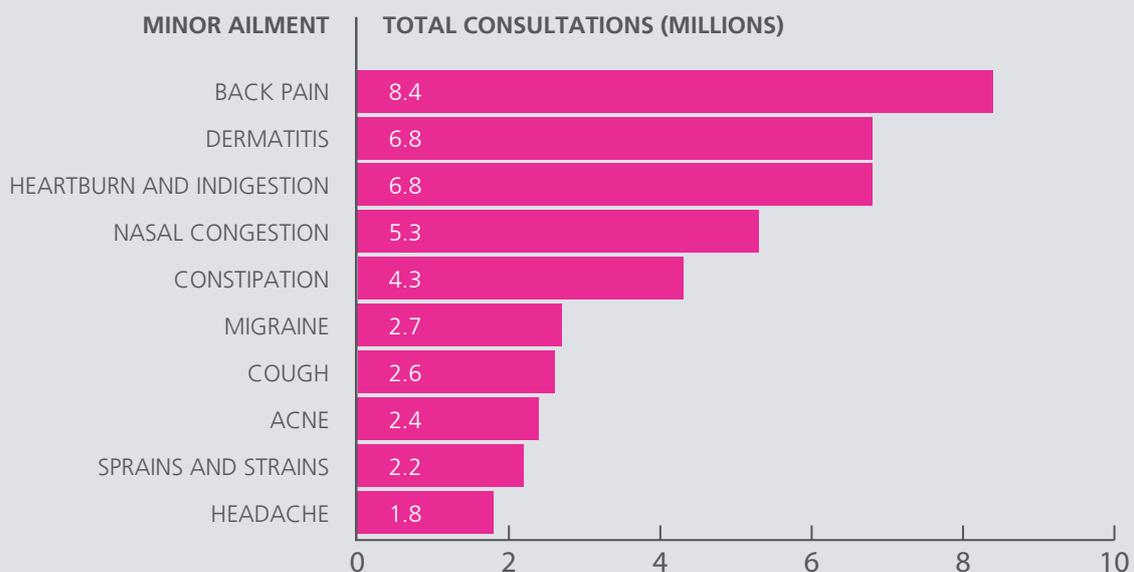
of prescription costs

amounting to **£1.6bn**, according to the study.¹⁰ A more recent study by IMS Health for PAGB (March 2015) showed that similar conditions treated in hospital emergency departments cost the NHS

£290m annually.¹¹



FIGURE 1: TOP 10 MINOR AILMENTS BY NUMBER OF CONSULTATIONS



“An industry-sponsored study by the consultancy Booz & Co in 2012 found that every dollar spent in the US on OTC drugs led to health-system savings of between six and seven dollars.”

The market has become increasingly global in recent years. Western Europe used to be the region with the highest OTC sales. However, several years of rapid growth (130% between 2009 and 2014) means that now Asia-Pacific outside of Japan is the largest market. Growth in recent years has been strongest in emerging markets, such as Malaysia, Indonesia and India, while market size has even declined slightly in some more developed countries, including Taiwan, South Korea and Japan.

Governments see various advantages in promoting the greater use of non-prescription drugs where safe. One is simple economy: “more and more the trend [in most countries] is to get drugs and medicines into the OTC category, where people pick up the tab themselves,” says Professor Thomas Szucs, head of medical economics at the University of Zurich’s Institute of Social and Preventive Medicine.

An industry-sponsored study by the consultancy Booz & Co in 2012 found that every dollar spent in the US on OTC drugs led to health-system savings of between six and seven dollars. It also estimated that 60m more people had conditions treated per year than would have in a hypothetical world where all drugs were prescription only.⁹ The potential for still greater savings, though, remains: Andy Tisman, senior principal at IMS Health, an information and technology services company, reports that research by his firm found that about one in five consultations with general practitioners and hospital emergency departments could have been handled through self-care in the UK.

However, the cost savings of switching drugs to OTC availability tend to be unevenly distributed. Research that looked at the drivers behind increased OTC availability, using examples from the UK, the US and Sweden, concluded that the switch from prescription to OTC “reduces insurers’ prescription drug costs but increases the costs for most patients”; the main motives for the switch identified in the research were “pharmaceutical firms’ desire to expand their market, attempts to reduce drug bills, and the self-care movement.”¹² Hence, while moving drugs from prescription-only to OTC may save costs for healthcare systems and open new markets for pharma companies, this does not equate to cost savings for patients.

Cost, though, is only one issue. Non-prescription drugs, by reducing the steps an individual needs to take to obtain medication, are by their very nature more accessible. The UK has a reputation for being among the most open to allowing pharmaceuticals to be classified as OTC.¹³ Dr Sarah Branch, deputy director of the Vigilance and Risk Management of Medicines Division at the UK Medicines and Healthcare products Regulatory Agency (MHRA), explains that behind government policy has been a desire “to widen access and support the whole concept of patient empowerment

and choice when it is safe to do so.” This has, for example, led to a shift to reclassification of types of drug that might not previously have been considered, such as those for long-term conditions.

This thinking, at least ostensibly, is not unique to the UK: “If you look at the reform agendas of many health systems,” says Michael Thomas, a partner in A.T. Kearney’s Global Pharmaceutical Practice, “they all talk about empowering the patient to take responsibility for their own health,” although the practice, he warns, is not always consistent with the sentiment.

However, making drugs available OTC does not necessarily empower patients. For example, Harry Cayton, the former chief executive of the UK’s Alzheimer’s Society, has argued that widening access to medicines is less important than the availability of credible information and patients’ ability to take responsibility for their own health.¹⁴ Patients may not always have sufficient knowledge to make informed decisions on OTC drugs. Moreover, patients are not necessarily disempowered in consultations with their doctor about prescription decisions.

Patient empowerment raises particular challenges for effective regulation because patients are far from a monolithic group. Kaisa Immonen-Charalambous, senior policy adviser at the European Patients’ Forum, explains that “every patient is an individual, and patient-centredness means care and services that are tailored to respond to the individual’s specific needs and circumstances.” Health literacy levels, for example, can vary widely even within societies. This makes questions of what information patients need in order to make appropriate decisions on OTC drug use – or how best to present this information – particularly complicated.

A web of inconsistent national regulation

Regulation is an inevitable part of any aspect of healthcare and, for good reason, non-prescription medication is no exception. Whatever the perceived benefits, the public health challenges of putting potentially dangerous drugs outside the control of medical professionals has led to a wide number of concerns and, accordingly, an extensive range of controls in most countries (see Figure 2).

Little research exists, however, to help guide policy-makers on the impact of specific regulations on the OTC market in terms of costs, access or safety. What is available tends to focus on the effect of particular regulatory options within states: recent literature reviews, for example, have found that increasing the number of drugs with OTC status tended to reduce prices and that liberalising the types of channels which could sell non-prescription drugs increased access slightly, although it had little impact on price.¹⁵

Instead of evidence-based policy, much regulation in this field relies on the specific health needs of individual countries, their ability to enforce regulation, current health authority thinking about the role of patients and doctors, or even traditional views in society about the effectiveness of certain substances. This results in substantial national variation between systems. In some cases, there is little regulation to speak of at all. **▶**

Chapter 1

Dr Vincent Ahonkhai, a senior adviser, Global Health Regulatory Affairs, at the Bill and Melinda Gates Foundation, says of Africa, that in practice in certain countries “virtually everything is non-prescription.” Mr Tisman adds that this is the case in many emerging markets: “lines are much more blurred as to whether there is OTC regulation at all and how easy it is to buy prescription drugs for cash without a prescription anyway.” Moreover, Mr Thomas says that in some emerging markets “the sorts of claims that are made for some medicines would simply not be allowed in the EU, which is trying to enforce an evidence-based culture on claims. There is rightly the need to strengthen regulations in some markets.”

At the other extreme, however, jurisdictions with extensive, well-enforced regulation often have their own weaknesses. Mr Thomas notes that OTC oversight systems in many developed countries have not caught up with the age of patient empowerment. Instead, they continue to reflect anachronistic assumptions that “healthcare decisions need to be mediated by a professional – a pharmacist or a doctor – and that patients cannot make decisions on their own. This is reflected in the language that can be used in advertising or packaging that does not connect with the typical consumer and the layperson’s knowledge of medicine.”

Such views rarely reflect distinct national cultural assumptions shared by patients. Ms Immonen-Charalambous notes, for example, that while some cultural differences “exist across the EU, our work with patient representatives from across the Union has shown clearly that the fundamental principles of patient empowerment are the same everywhere.” Instead, the variation in regulation arises from differences in opinion on the appropriate level of power patients should have, and are able to assume, in their own healthcare.

Marked regulatory differences, even between countries in the same region with similar levels of development, have helped to create international fragmentation in the OTC market. For example, Europe has only a handful of active ingredients available over-the-counter in every country.

“the regulatory inconsistency is a challenge for the industry’s ability to drive innovation and bring it to market.”

Andy Tisman, IMS Health

FIGURE 2: THE BUILDING BLOCKS OF OTC REGULATION

As with most of healthcare, the non-prescription drug market is shaped by extensive regulation. Frequently, the specifics differ by jurisdiction. Moreover, convergence in just one or two areas may do little to alleviate overall market fragmentation. The most important areas of regulation typically include:

Permitted products:	what a company is allowed to sell on a non-prescription basis, including the classification of pharmacological active ingredients at a given dosage as OTC, as well as the re-purposing of previously classified ingredients in other products, such as adding an OTC painkiller to a cough syrup;
Required data:	what information is needed by the relevant authorities making the original classification decision or permitting additional uses;
Market exclusivity:	the period during which the company applying to switch an active ingredient from prescription only to OTC status may sell it without competition;
Manufacturing practice and quality:	the standards that those making a product must meet and maintain;
Channels:	the type of merchants through which an OTC product can be sold, which may include pharmacy only, general sale, or some intermediate channel;
Claims:	what marketing can say the product will do, and where they can say it;
Labelling and inserts:	what claims OTC packaging is allowed make, the information it needs to give about correct usage and contraindications, and the extent to which that information is comprehensible to a non-expert;
Pricing and reimbursement:	the extent to which OTC drug prices are controlled or those purchasing them are able to get any financial assistance with the cost – normally, in the latter case, through a medical professional issuing a prescription for it;
Drug safety (pharmacovigilance):	how negative outcomes from usage of the drug need to be reported.

RB Viewpoint

Wider impact of inconsistent regulation

Consumer-centric innovation is at the heart of everything we do at RB and our unique approach to innovation enables us to provide safe, effective solutions designed specifically for our consumers' needs. There are products which need not be subjected to the highest level of regulation. For example, Strefen/Strepsils containing the active ingredient flurbiprofen, is an effective treatment for sore throat of which there are few good alternatives. This product has been the subject of various regulatory challenges including branding and format issues which ultimately hamper access for consumers. Inconsistent regulation means that 'umbrella branding' which can help consumers recognise and identify trusted brands is not supported by some authorities. Additionally, the scientific evidence required to approve the spray format of Strefen for over-the-counter use, varies from one country to the next. The impact of the lack of logical harmonisation here is twofold. Firstly, people are being denied optimised access to a product for a condition that is easily self-managed. Secondly, there is a wider financial and social impact. Primary care health service resources could be saved by people accessing appropriate care through the pharmacy. It's also reasonable to expect that by achieving symptomatic relief with such a product, the request for and prescribing of antibiotics would be reduced and preserved.

Variations in which drugs can be sold without a prescription have an effect on market cohesion. Other fields of regulation can have just as profound an impact. Sales channels, for example, fundamentally affect branding and marketing strategy. As Professor R. William Soller, editor-in-chief of the academic journal *SelfCare*, notes: "if you put a health professional between the drug maker and the consumer, then the pharmacist would be in control of product recommendations. Those might go to the store brand because it is generic." Accordingly, American OTC drug makers, which have a long tradition of direct-to-consumer marketing, have campaigned successfully since the 1880s to prevent a pharmacist-only drug category. By contrast, in some European countries the large majority of non-prescription drugs need pharmacist consultation before sale.

Helen Darracott, deputy chief executive at the PAGB says that even apparently small regulatory differences can make it impossible to have consistent packaging. Some European countries, for example, have a blanket policy of not approving OTC drugs for migraine headache treatment. As a result, non-prescription painkillers permitted for other uses in those countries cannot mention this condition in their labelling or marketing, even if approved for such a use in another member state. "It is not straightforward even to have a common package between countries with the same language," she adds. "Things like that should be easier."

Economic costs of regulatory disharmony between countries

If data is scant on the impact of national OTC regulation within countries, it is non-existent for the effect of regulatory disharmony between countries. Experts interviewed for this study, though, note that some resultant problems are obvious. "Economic costs are there," says Hubertus Cranz, director-general of the Association of the European Self-Medication Industry (AESGP). "If you have to duplicate certain activities, it is more expensive. Where classifications and trade names are different, there are costs." Ms Darracott agrees: "if you are running parallel procedures, you are introducing additional complexity, risk, and cost."

One study of innovative prescription drugs in Europe found that simultaneous approval could lead to overall earlier revenues for firms worth anything from €35m (US\$40) to €100m per drug.¹⁶ Given price differences between the prescription and OTC markets, and that most potential OTC products are usually available as prescription drugs before a change of status, these data is not directly comparable, but it does suggest that the economic effects of delays in the pharmaceutical field are often more than trivial.

It is not simply a question of economic burden. Regulatory differences also impede drug access. Mr Tisman adds that "the regulatory inconsistency is a challenge for the industry's ability to drive innovation and bring it to market." The next chapter will examine a number of initiatives to reduce unnecessary differences in regulation.

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An overview of four global and regional regulation harmonisation efforts

Stand-alone multilateral initiatives to harmonise non-prescription regulation as a whole do not exist. Improvements in recent decades have instead occurred in the context of other efforts that have had an impact on some – but not all – of the rules affecting the sector.

Such endeavours tend to arise in two distinct ways. First, various multinational and regional fora have appeared, aimed specifically at minimising the sometimes wide regulatory differences across borders facing the pharmaceutical industry as a whole. The hope is usually to accelerate drug development and approval, thereby improving access. These initiatives typically focus on questions amenable to science and therefore objective decision-making – such as measurement and assessment of efficacy, safety, and quality. Much of the effort, such as aligning requirements for the registration of innovative drugs, is tangential to the OTC industry, but various issues covered – such as manufacturing practices – are relevant.

Second, free trade areas are also wrestling with removing barriers to the flows of goods between countries, including pharmaceuticals, both prescription and non-prescription. Although in theory, these efforts could deal with any number of the market-related differences facing OTC sales, such as channels and labelling, in practice they have tended to stick to the same ground as the initiatives in the other category. The difference is that the existence of free trade or economic union treaties has provided an extra impetus to push through the sometimes difficult obstacles to harmonisation. ▶



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Two global initiatives

The most important effort at the global level is the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). Since 1990, this project has brought together regulators from many jurisdictions – including all the major ones – and industry participants. Although it has no formal legal authority, its guidelines and templates on matters of quality, safety, efficacy and relevant multi-disciplinary issues are very influential in shaping national and regional regulations.

Professor Soller explains that the templates do not lead to complete harmonisation so much as minimise differences. For example, the ICH's electronic common technical document could be used to share data on studies or meta-analyses of drug use from one country. If another country believed that the product in question would be used in the same way, it could avail itself of the information but if, for example, ethnic differences in its population or dietary differences might lead to different outcomes, it could require more data before making a decision on approving a substance. Nevertheless, such an approach is superior to having a completely new technical document for each country.

Not all the work of the ICH is relevant to non-prescription pharmaceuticals, but its Expert Working Groups on Quality and Efficacy have had OTC industry representatives since 1996 in recognition of the potential impact of decisions in this area. Professor Soller recalls that, before ICH's appearance, even expanding the use of aspirin – a longstanding OTC drug in many jurisdictions for pain relief – to cover heart-attack prevention required specific national trials in a lot of countries despite good evidence from similar populations elsewhere. Nevertheless, ICH covers only a very limited part of the regulations facing the industry.

The other notable international initiative has a similarly tight focus. The Pharmaceutical Inspection Co-operation Scheme is an informal agreement between health agencies from 43 different countries – with an additional seven likely to join soon – aimed at promoting common standards of good manufacturing practice, high levels of oversight competency, and mutual recognition of inspection of production facilities. However, the history of the scheme shows the hurdles that can come up in promoting regulatory harmonisation. The current, informal arrangement was adopted in the mid-1990s after efforts to expand a formal convention on pharmaceutical inspection dating back to the 1970s was found, for technical reasons, to violate EU law.

Current efforts at this level, then, while able to remove important inconsistencies for the OTC market, deal with only a limited part of the regulatory burden.

Two regional initiatives

In addition to global efforts, several regional efforts have tried to improve harmonisation of rules around pharmaceuticals. One, dating back to 1999, is the Pan American Network for Drug Regulatory Harmonisation (PANDRH). While delegates to the body are identified by individual country

and participate through national regulatory authorities, they also act as representatives of one of the six trading blocs present in the region. Furthermore, although Canada and the US participate, the effort is largely a Latin American one.

The aims of the body are to improve access to high-quality drugs and to improve technical cooperation and assistance between regulatory agencies in the Americas. Atypical of the other initiatives in this field, PANDRH has made specific efforts to consider harmonisation of regulations surrounding OTC pharmaceuticals. In particular, after two years of study, in 2005 it approved a document on the definition of such medications, criteria for classifying drugs in this category, and criteria for associated promotional material.

However, the impact of this aspect of PANDRH's work over the last decade has been small, and the topic has fallen off the agenda. After presenting its report in 2005, the original OTC Expert Working Group wound up its activities, and one on marketing and promotion – which took over monitoring results of the former's work – has met infrequently. This, according to PANDRH's 2014 Operations Report, is because the country responsible for chairing meetings has not nominated a representative in some years, although in practice this may simply reflect low interest among governments in working collectively on the issue. Meanwhile, only a handful of countries have incorporated elements of the 2005 working paper into national regulations.

Dr James Fitzgerald is director of health systems and services in the Pan American Health Organisation (PAHO), which is both the WHO's regional office and the specialised agency for health within the Inter-American System. He explains that this result shows one of the challenges with the forum: "PANDRH is not a binding, but a consensus-building, forum. Countries may agree to, but may not completely implement, what has been recommended. This has led to a rainbow of results in terms of degree to which recommendations have been implemented."

Moreover, the rather meagre outcomes of the OTC working group – its recommendations covered, in total, under two pages – were in many ways an attempt to achieve common ground where a marked variety of views exist. Dr Fitzgerald sees "significant cultural differences between the perceptions of the role of the regulatory authority vis-à-vis the market. Some countries firmly believe that there should be a tendency toward free sale, shifting the responsibility of use to the consumer; others believe the public health authority should ensure more stringent regulation."

The difficulties with non-prescription drugs are consistent with some of the issues which have led PANDRH to rethink its role. In the first few years of its operation, it became apparent that creating harmonisation when such vast diversity existed in the functional capacity of national regulators was like running before one could walk. Instead, Dr Fitzgerald reports, "we took a step back to see what kind of capacity was needed." This has entailed a focus for the last decade in helping to build up national regulatory systems in a way that will build trust between them and, based on shared principles, will lead, ideally, he says, to eventual regulatory convergence. "It is not

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harmonisation, but more a progressive process by which cooperation between countries builds the necessary confidence to get there.”

Dr Fitzgerald notes that the region has seen substantial progress in building up national capacity. Nevertheless, ongoing political and capacity differences mean that harmonisation, including in OTC regulation, remains distant.

A more recent continent-wide initiative is the African Medicines Regulatory Harmonisation (AMRH) Programme. Like PANDRH, it involves collaboration among regional economic communities, but also has a significant partnership with international funding and development agencies and NGOs including the World Bank, the UK's Department for International Development (DFID), the Bill and Melinda Gates Foundation, and the Clinton Foundation.

AMRH's emphasis is squarely on public health in Sub-Saharan Africa. Dr Ahonkhai, who leads the Bill and Melinda Gates Foundation's work with the programme, explains that “the entire vision of the initiative is to accelerate access to health products in some of the poorest countries of the world, particularly in Africa.” Here, inconsistent regulation is more than inconvenient; it is lethal. “The problem to date has been lengthy regulatory review times and therefore delays that reduce access to health products. That delay definitely has an impact on morbidity and mortality statistics,” he adds.

The focus has been on assisting regional economic communities to work together, not just on harmonising standards but on joint decision-making. Given inevitably limited resources, the initial focus has been on the registration of medicines and vaccines. Dr Ahonkhai notes that, unlike in some parts of the world, sovereignty has proved less of a barrier to harmonisation than might have been expected. As mutual understanding and trust between agencies has grown, “countries have actively started to work together. This has never happened before [in Africa on pharmaceutical regulation]. They have even started to register products together.” This is partly through necessity: many countries lack the resources and expertise to adequately create and oversee effective regulation in this field on their own. Nevertheless, Dr Ahonkhai believes that the pressing need for better access is prompting governments to make faster progress on harmonisation than some other parts of the world have seen.

AMRH is also addressing quality. Dr Ahonkhai explains that “this is perhaps the most critical aspect of medicine in lowest-income countries” where sub-standard or even counterfeit drugs are common. Manufacturing regulations are being standardised in several economic communities, and countries are moving toward mutual recognition of inspections of production facilities. Meanwhile, supply chain standards are, he says, “next in line to fix.” East Africa, in particular, has begun work in this area.

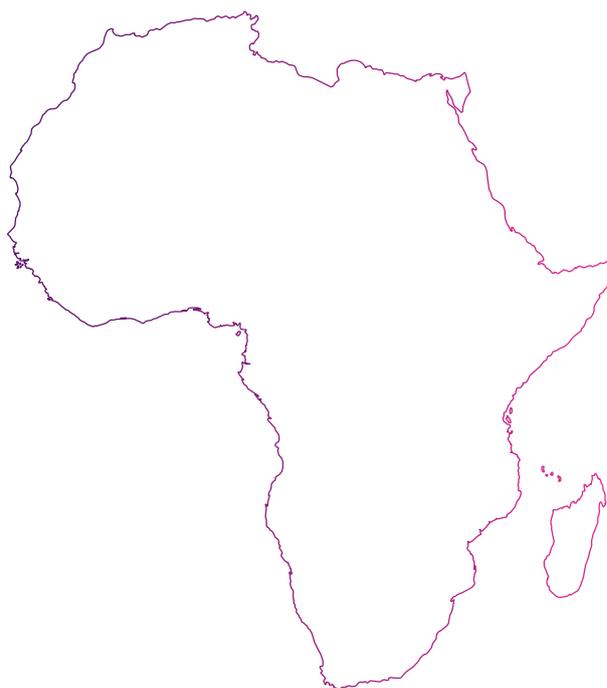
OTC drugs are not directly addressed by AMRH and classification questions, nor are they likely to be on the agenda soon. Nevertheless, says Dr Ahonkhai, the nature of drug distribution channels in Sub-Saharan Africa makes the work on quality highly relevant to the field of OTCs. “For the

vast majority of drugs,” he says, “to go anywhere and pick up what you want is the norm in most of Africa. Getting those products to be of good quality, irrespective of how you acquire them, would be a huge accomplishment in terms of access to the right product.”

Rather than regulatory disharmony around OTCs, then, much of Africa faces a regulatory vacuum. With so much to address, harmonisation efforts are unlikely to fill this soon, but their work can reduce some of the negative consequences.

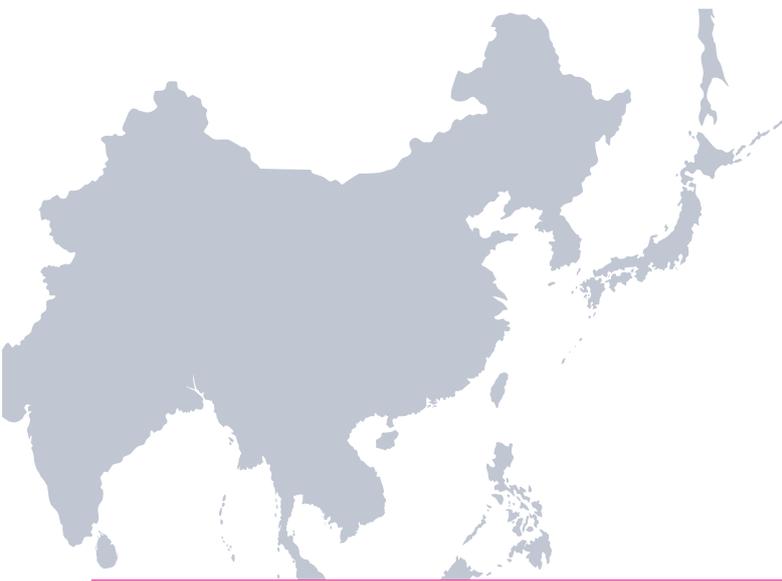
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Dr Vincent Ahonkhai, Bill and Melinda Gates Foundation



A closer look at regulation harmonisation efforts in ASEAN and the EU

Two economic regions in particular, the Association of Southeast Asian Nations (ASEAN) and the EU, have the most extensive experience in trying to harmonise pharmaceutical regulations. The experience of both is illuminating in looking at the possibility of, and barriers to, progress.



“[Officials have] taken the very pragmatic approach that they are building a model to ensure consumer safety but also to ensure investment and development. They are looking at regulation as a way to increase confidence for companies to invest.”

Simon Pettman, International Alliance of Dietary/Food Supplement Associations

ASEAN: steps toward partial regulatory harmonisation

Healthcare, including the pharmaceutical sector, is one of 12 priority sectors for ASEAN economic integration. Discussions about pharmaceuticals began in earnest in 1999 with creation of the Pharmaceutical Product Working Group (PPWG) – a group of national representatives which now meets at least annually – within the ASEAN Consultative Committee for Standards and Quality.

The PPWG’s work aims at the removal of technical barriers to trade in pharmaceuticals as a whole. Its specific focus has been on data, quality, effectiveness, and safety related to drug registration and manufacturing. There have been three main results. First, an ASEAN Common Technical Dossier (ACTD) creates a common format and structure for applications for drug marketing authorisations in all member states. Second, the ASEAN Common Technical Requirements (ACTR) is a guide that describes for applicants the common expectations of pharmaceutical regulatory authorities in member states when deciding on marketing authorisation. And third, a Mutual Recognition Arrangement (MRA) for Good Manufacturing Practice (GMP) certificates and inspection reports issued by the national authorities for individual drug-production facilities has been identified as a priority initiative.

The goal has been not just to create ASEAN-wide standards, but to harmonise regional practice with global practice. According to Dato’ Eisah Binti A. Rahman, senior director of pharmaceutical services at the Malaysian Ministry of Health, “we referenced ourselves in everything we do with international standards and systems in place. The technical dossier, for example, is very much based on that of the ICH.” Similarly, the ultimate goal is for all member states to adopt as manufacturing standards those in the Pharmaceutical Inspection Co-operation Scheme; however, as yet, only Singapore, Malaysia, and Indonesia are full members of that agreement.

The results so far represent no mean achievement. Working in ASEAN, practical differences of nine national languages in 10 countries are a given, but a bigger issue facing negotiators was lack of knowledge about each other. Dato’ Eisah recalls that “prior to 1999, we really didn’t know what our neighbours were doing. When we got together we realised how differently other countries were doing things.”

Another strength of the process has been co-operation between regulators and industry – something previously unusual in ASEAN countries. Simon Pettman, executive director of the International Alliance of Dietary/Food Supplement Associations (IADSA), who has been actively involved in a parallel process in the supplements segment, says that officials have “taken the very pragmatic approach that they are building a model to ensure consumer safety but also to ensure investment and development. They are looking at regulation as a way to increase confidence for companies to invest.”

Anecdotal evidence suggests that harmonisation efforts have also had some positive effects. Dr Pathom Sawanpanyalert, deputy secretary-general of Thailand’s Food and Drug Administration, reports that adoption of the

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ACTD and ACTR has sped up drug registration in certain cases, and Dato' Eisah says that some 4,000 products have been registered in Malaysia by Singaporean drug manufacturers – a sign of improving access.

Major issues still impede effectiveness of harmonisation

Nevertheless, the overall effectiveness of ASEAN's harmonisation remains to be seen. As Mr Cranz notes "ASEAN countries reached very relevant agreements, but it is not evident what this will mean in day-to-day practice." Part of the issue is one of resources. Dato' Eisah points out that levels of development in ASEAN are highly varied. While Singapore, for example, clearly has resources to implement new regulatory structures, some of "the least developed countries do not have proper laboratories, officers, or computer systems." Implementation may take far longer in these states.

Moreover, the harmonisation of laws will not necessarily lead to the harmonisation of results, especially as a common dossier does not create a single decision-making process. Instead, 10 different governments may decide on the same information. Mr Tisman explains that "with people who are willing, harmonising regulation may certainly be possible, but how they are interpreted country by country can be a huge challenge." Dato' Eisah agrees: "you may have a common document, but if each country interprets it differently, you will not have convergence. You may not come to a harmonised understanding." The extent to which this will occur, remains to be seen as the new rules are fully put into practice.

Malinee Uditananda, chair of the Asia-Pacific Self-Medication Industry (APSMI), highlights a red flag that has already appeared: the existence of agreed, common ASEAN technical documents has not prevented the introduction of diverse additional regulations in individual countries: "these country-specific requirements have been increasing in the past few years. We hope that the PPWG will, keeping to the spirit and original intention of harmonisation, try to minimise them." Doing so may not be straightforward. Mr Cranz says that Europe's experience shows "you need a body which is supervising the agreement, in order to enforce implementation." ASEAN, however, as an economic, consensus-driven rather than political-economic entity lacks this feature.

An even bigger issue is that "OTC or non-prescription drugs have been regarded as the simple category and put together with generic medicines," notes Ms Uditananda. "Therefore, they have not been given priority in terms of regulatory harmonisation."

As a result, drug classification criteria and procedures remain entirely national concerns. As Dr Sawanpanyalert puts it, "one of the major [existing harmonisation] issues is that some OTCs in one country have to have a prescription in others." He expects that in future ASEAN may seek to address the question, but for now this is purely a matter for member states. More generally, the large majority of OTC regulation in ASEAN countries remains purely national. Permissible channels vary – Thailand, for example, has a pharmacist-only category (so-called "dangerous drugs") within

pharmacies, and another for wider sale by pharmacies ('ready-packed drugs'), while in Indonesia all non-prescription drugs limited to pharmacy sales have the same status. Matters of labelling and claims also vary.

Looking beyond regulation, other issues drive market fragmentation in Asia, as elsewhere. The healthcare needs, and health literacy, of a Singaporean are likely to be far different from those of a Laotian. Cultural expectations also vary widely. Mr Tisman points to studies showing that in the Philippines a large majority of those entering a pharmacy to purchase a non-prescription product expect to make the selection themselves, while most going in such a store in China expect to get advice from a pharmacist.

The PPWG, however, did not look at broader cultural or stakeholder matters but focussed closely on issues amendable to scientifically determined best practice. Indeed, beyond regulators and industry, other potentially interested parties – such as medical professionals or patient groups – have not been part of the process. While this has helped ASEAN achieve progress in specific areas of regulatory harmonisation, it has left unaddressed much of the regulation that affects non-prescription drugs.

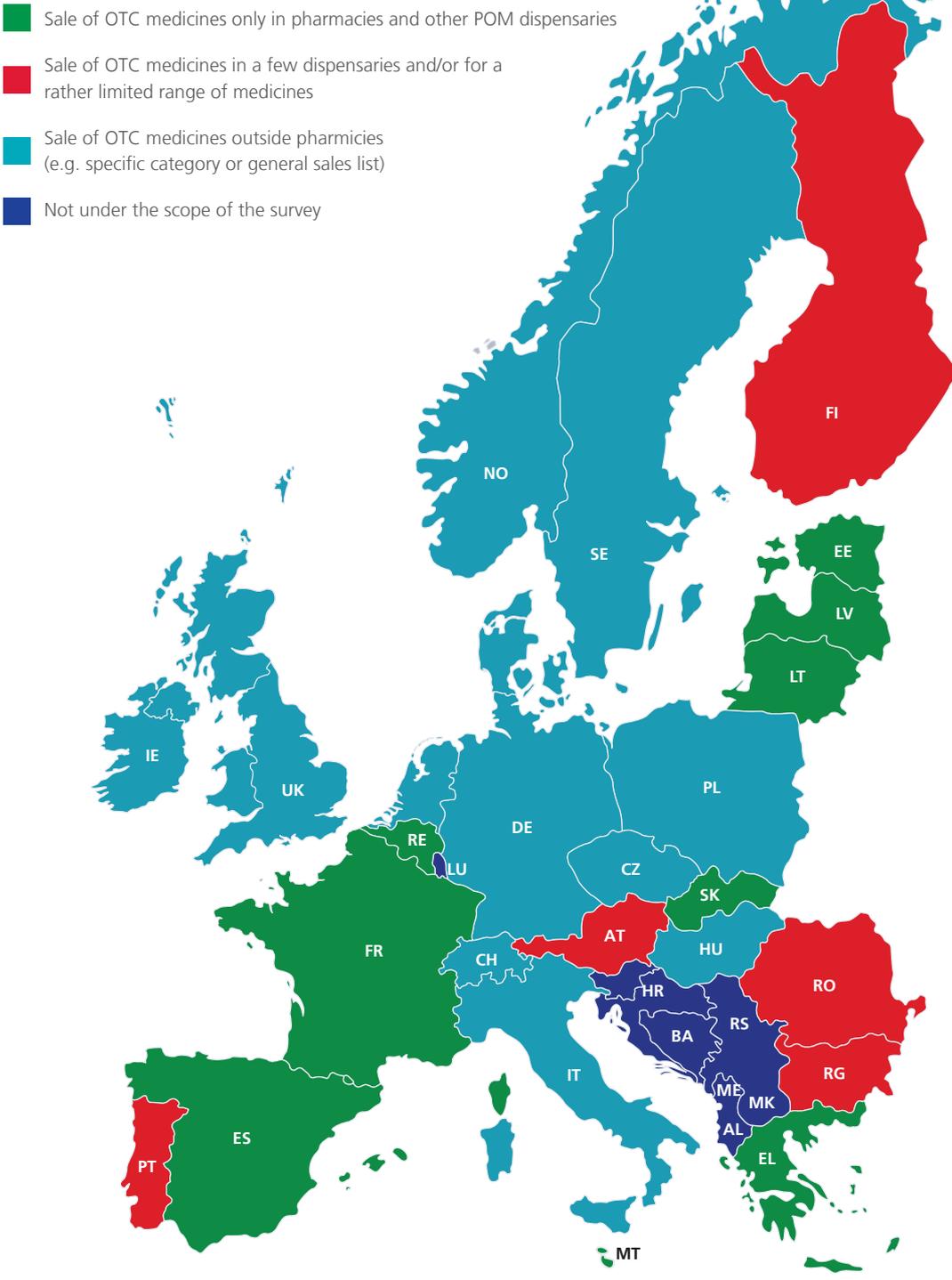
The EU: the practical limits of regulatory harmonisation

European law to harmonise pharmaceutical regulation goes back to as early as 1965. The core current legislation in this field, EU Directive 2001/83/EC, dates to the beginning of this century and, although amended from time to time, its main elements largely remain in place. Even after 50 years of ostensible convergence, though, the OTC marketplace and regulatory environment are still markedly fragmented on national lines. As Mr Tisman puts it, "there is a mass of different national licenses, and different legal situations in terms of distribution and promotion." Professor Szucs expects little further progress in the region, saying "OTC regulations will always be much more non-harmonised than harmonised. I foresee huge diversity in terms of market scope and penetration of OTC medications."

One reason for disharmony is that European law does not cover all aspects of regulation. Mr Cranz divides the field into three: "there is a high level of harmonisation in anything around market authorisation or registration. Then, there is a middle level for rules around classification and promotion. Fundamental rules exist, but the final decision is left to the member state. The lowest level of harmonisation is on issues around distribution channels, pricing, and reimbursement."

The lack of common legislation in the last of these groupings leads to a sometimes bewildering array of regulatory differences. The most visible diversity is in sales channels which, as the map below shows, vary widely across Europe. Even this map, though, simplifies matters: although it puts Italy, the UK, and the Netherlands in the same category, the Netherlands does not permit OTC sales in convenience stores and Italy does not have specialist drugstores that are distinct from pharmacies, while the UK allows non-prescription sales in both these channels. As Mr Cranz puts it, this is an area "where you have different views and where, for the time being, there is no way Europe will step in." ▶

Figure 3:
Sale of OTC medicines outside pharmacies in 28 European countries



Specifications regarding sale of OTC medicines in a few dispensaries and/or for a rather limited range of medicines:

- AT:** Drugstores: sale of a rather limited range of OTC medicines
- BG:** Drugstores: sale of a selected range of OTC medicines. Vending machines (owned by pharmacies or drugstores); less than a dozen of OTC medicines
- FI:** Pharmacy service outlets: service points for a range of OTC medicines under the supervision of a pharmacy in rural areas; retailers and vending machines for Nicotine Replacement Therapy (NTR) products if OTC
- PT:** Specific OTC dispensaries: sale of OTC medicines in these OTC dispensaries;
- RO:** Drugstores: sale of OTC medicines

Source: Vogler, S., "Liberalization in the Pharmacy Sector," 2014.

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Other key factors affecting access and sales are equally diverse. In seven EU countries it is never possible for a patient to receive reimbursement for an OTC medication, in five it is permitted with a prescription, and in the rest it is possible but under very restricted conditions.¹⁷ Even the number of tablets of the same drug available in a package can differ dramatically. Professor Szucs notes that for some products this can differ from 16 to 200 depending on the jurisdiction. “Local sales rules are a long way from being harmonised; I don’t think they will be,” he concludes.

More surprising is the relative lack of a harmonised operating environment in practice where common European regulations exist. EU Directive 2001/83/EC, for example, states that, with certain restrictions, advertising of OTC products is permitted. However, a review by the European Forum on Advertising Medicines, a joint initiative of regulatory bodies, found a range of different regulatory approaches to marketing of non-prescription pharmaceuticals, including inconsistent restrictions on the use of television and radio as opposed to print.¹⁷

The most striking area where common rules have led to wide variance in outcomes is product classification. A basic element of a harmonised international regulatory environment is that the same goods are available in each country. By this standard, the European market in non-prescription pharmaceuticals remains very far from unified. Ms Darracott notes that what is permitted on sale without a prescription in EU states “is hugely different.” As of 2011, only five ingredients were available over-the-counter in some form across Europe as a whole and, since then, just two more have been added. Even a substance such as ibuprofen, which was first approved for non-prescription sale in the UK in 1983 and is widely available OTC in Europe, still requires a prescription in Bulgaria, for example. A Centralised Procedure allowing simultaneous approval across the EU, meanwhile, has been less effective than initially hoped (see box opposite).

The Centralised Procedure: when theoretical harmonisation meets practical realities

The diversity in which ingredients may be sold over-the-counter in Europe does not surprise Hubertus Cranz, director-general of the Association of the European Self-Medication Industry (AESGP). “If the decision on prescription-to-OTC switch is with member states, it is not surprising that they do not always come to the same conclusion.” Nevertheless, European institutions have made efforts to create greater similarity of outcomes. Traditionally, companies have had to apply to each relevant national regulatory authority separately for permission to sell their product over-the-counter. This is still possible. Moreover, to make applications easier after an initial success, European regulations provide a mutual recognition procedure: a company can take an approval in one member state and use it to speed up evaluation by authorities in other countries, although the latter still have the ability to refuse market authorisation.

A theoretically more appealing option, however, has existed since 2007. Businesses can choose the so-called Centralised Procedure. In this situation, a decision on the suitability for non-prescription status is made at the European level by the Committee for Medicinal Products for Human Use under the authority of the European Medicines Agency. If the application is successful, the ingredient receives immediate market authorisation across the entire EU and can be sold under a single trade name with common labelling and package information. This brings obvious advantages in terms of reduced paperwork in the application process and the ability to rapidly build a Europe-wide product brand at far lower cost than slowly rolling out across the continent.

When the Centralised Procedure was made available, the general expectation was that it would have a major impact, according to Andy Tisman, senior principal at IMS Health, an information and technology services company. However, he says that the reality has been disappointing. Since 2007, only four ingredients have received market authorisation under the procedure. Put in context, just three active substances – paracetamol and acetyl salicylic acid (mild pain killers) as well as topical ketoconazole (a fungicide in skin creams) – have achieved universal OTC status in Europe through decisions by all national regulators. Already more have done so with the Centralised Procedure. On the other hand, in the decade before 2012, every year on average six new active ingredients obtained non-prescription status in at least one Europe country. In short, the Europe-wide option is having only a small effect on the market.

Lack of uptake by companies is a major reason for the low impact of the Centralised Procedure. In addition to the four approvals, three applications have been rejected or withdrawn. Dr Sarah Branch,

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deputy director of the Vigilance and Risk Management of Medicines Division at the UK Medicines and Healthcare products Regulatory Agency (MHRA), points out that smaller companies may find a European level application more daunting than a national one. She adds, though, that the European Medicines Agency has an office to assist SMEs in this area.

The bigger issue, however, is that differences in attitude toward the balance of patient risk and benefit, as well as the vast diversity in how OTC drugs are sold across the EU, inevitably affect the outcome of the process. According to Helen Darracott, deputy chief executive at the Proprietary Association of Great Britain (PAGB), a consumer healthcare industry organisation, the resultant problem “is gaining consensus around a product that actually will be commercially viable. What worries companies about going down this route is the danger of reaching a lowest common denominator, with the safest and most non-controversial option.”

Two failed applications illustrate the difficulties. Sumatriptan was rejected as a possible OTC migraine treatment because of the risk of overuse, misuse, or misapplication if available without a prescription. However, at least six European countries, including France, Germany, and the UK, have allowed sale of either sumatriptan or other triptans over-the-counter for a number of years, some for nearly a decade. Presumably, the majority of national experts on the European Medicines Agency panel reviewing the application had different views on risk to those of their colleagues in these countries.

Meanwhile, the rejection of sildenafil (which is used to treat erectile dysfunction) for a European Market Authorisation resulted from concerns about the way that different practice in the pharmacies of individual member states meant that some would be unable to dispense the product safely even though others would.

Even success with the Centralised Procedure does not always remove every blockage to market access. The recent approval of ulipristal acetate, a morning after pill, for OTC status might still have faced complications had the authorities in any country opted to use exceptions in EU law allowing restrictions on the use of contraceptive medicines.

The weaknesses of the Centralised Procedure, however, will soon need to be addressed. An increasing number of prescription pharmaceuticals have received marketing authority in this way since it was established, and the EU has ruled that for such medicines, the only route to OTC status is via a further Centralised Procedure application. As the muted use of the procedure to date shows, though, regulatory harmonisation is far more than a matter of putting in place a common set of rules that cover one aspect of the market.

The difficulty is not in the rules themselves. As Dr Branch says of the prescription-to-OTC switch, “the actual laws, the regulations, are harmonised because the criteria for prescription-only medicine are in EU legislation.” Ms Darracott agrees: “the law is harmonised. There aren’t differences; in terms of safety and efficacy profile, it is the same.”

Part of the problem is that, given the large number of regulatory fields that affect the non-prescription drug market, basic inconsistencies in some areas will impede harmonisation of others. One weakness of the Centralised Procedure has been that different levels of pharmacist involvement in distribution of non-prescription products has affected views on the safety of putting given products on sale across the EU.

Labelling is another issue. Directive 2001/83/EC addresses the content requirements of OTC labels and pamphlets. However, a recent set of guidelines issued by the European Medicines Agency acknowledges that, because of different supply arrangements for these products, “national practices on pack design for non-prescription medicines differ across member states,” including necessary symbols and pictograms as well as information in the Summary of Product Characteristics.¹⁸

Nor does harmonisation mean that rules are necessarily fit for purpose. Clear information around OTCs is essential for patients and, accordingly, European regulation covers the requirements for the patient information leaflet (PIL) included with medicines. Ms Immonen-Charalambous notes, though, that “despite incremental improvements over recent years, the PIL is still widely agreed not to be patient-friendly and many patients do not even read it. A recent study in England found that a third of older adults had difficulties reading and understanding the instructions on a packet of aspirin. Poorer understanding was associated with higher mortality.” She adds that the EU undertook a review on the shortcomings of the standard PIL in 2013 but that the results have not yet been published, even though under the 2011 EU pharmacovigilance (drug safety) legislation it is required to make recommendations for improvements. ▶

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Cultural differences

The bigger issue, however, is that the same cultural differences that give rise to a variety of distinct national approaches in inconsistent regulatory fields also lead to diverse interpretations of common rules in harmonised ones. In particular, says Mr Tisman, these reflect fundamental “cultural differences across the region as to the perceived role of the doctor or the pharmacist and the acceptance of self-care,” with many professionals still not trusting patient judgement. “At the end of the day, the main barrier to harmonisation is that the mind-set around self-care – the acceptance of what responsible self-care and patient empowerment mean today in concrete action forms – is not identical,” adds Mr Cranz. “Some countries are open to change; others have a fundamental scepticism. The change from prescription to OTC, for example, is formally a scientific consideration. The law is good, but there is a level of interpretation and some tend to be more careful, others more open.”

Europe’s fragmented OTC regulation, then, is not a cause but a symptom. Improvements in specific areas, especially in areas where science can provide objective criteria, can help at the margins. Nevertheless, a harmonised non-prescription drug market will need to reflect more harmonised views around their appropriate role in healthcare and the best way to balance risk and reward from greater patient empowerment.

As the examination of the European situation in particular shows, though, improvements that affect only a limited part of the regulatory environment will not lead to a unified market. Moreover, regulatory variations between countries often reflect deeper cultural assumptions that would induce substantial fragmentation even where formal laws are identical. These difficulties are not restricted to the OTC market. Many parallels exist between regulations on OTC drugs and those on food supplements, for example. Neither seems to have found a way to create a truly international regulatory environment and market (see box).

A wider look at consumer healthcare: the regulatory challenges of dietary supplements

As with the non-prescription-drug market, supplements face “quite a long list” of inconsistent areas of regulation, notes Simon Pettman, executive director of the International Alliance of Dietary/Food Supplement Associations (IADSA). These include those familiar to other parts of consumer healthcare, including: mutual acceptance of good manufacturing practice between countries; the need to re-test for product safety and stability in new countries; and potential huge delays of approval and pre-market clearance. The biggest disparities, however, revolve around two basic issues, he says: ingredients and claims.

The differences can be extensive as the example of St John’s wort, a medicinal herb used to treat depression, shows. Even within Europe its status varies. In some countries, it is readily available as a herbal supplement, others regulate it as an OTC drug, and some – notably Ireland – require a prescription.

The disparity around claims can be just as diverse. Although European regulations contain a list of specific, permissible claims about food supplements – including vitamins and minerals – in Japan, notes Michael Thomas, a partner in A.T. Kearney’s Global Pharmaceutical Practice, no labelling and advertising claims have historically been permitted. The result, he adds, is use of different, direct selling models: “one reason that there is so much direct, door-to-door selling of vitamins and supplements in Japan is that it is the only opportunity to differentiate products; it is difficult to regulate what agents are going to say face to face when they knock on a door. Regulations are now changing, which may lead to the ability to build brands in a more conventional way.”

As with non-prescription drugs, several regions are trying to bring greater standardisation to regulation of food supplements. These include the Pacific Alliance – a Latin American trade group consisting of Mexico, Peru, Chile and Colombia – and the Eurasian Customs Union, made up of Russia, Belarus, Kazakhstan, Armenia, and Kyrgyzstan. As with OTC drugs,

though, the most advanced efforts are those in the EU and the Association of Southeast Asian Nations (ASEAN).

After more than a decade of effort, though, the situation in the EU remains decidedly mixed. On the one hand, as Mr Pettman puts it, “what is harmonised is well harmonised.” This is particularly the case for vitamins and mineral supplements. In contrast, botanicals – such as herbal supplements – and amino acids remain regulated largely at the national level. Here, explains Mr Pettman, “you have some substantial variation in position” over questions of safety and efficacy. The difficulties tend to be as much cultural as purely scientific, but are deep-seated. German-speaking countries in particular tend to set great store in herbal remedies and supplements.

There are steps towards creating some common ground: in recent years Belgium, France and Italy have adopted a largely harmonised list of 1,000 botanicals that can be included in food supplements. The bigger picture, though, is one of diversity. Mr Pettman expects little change, as the political will is lacking. Indeed, a 2013 UK government report even suggested that this was a field where harmonisation might not be appropriate or helpful.¹⁹

By contrast, in ASEAN the common cross-regional regulations that the trade bloc has developed are, in Mr Pettman’s view, “very solid.” He praises the approach to the harmonisation talks that included officials from ministries with oversight of food and pharmaceuticals, thus ensuring a higher level of buy-in. Moreover, he adds, those involved were concerned about both consumer safety and the needs of industry. Now, however, as with OTC drugs, “the next stage will be implementation of measures that took 10 years to agree. We don’t know yet what that will look like.”

Despite the benefits that greater regulatory harmony might bring, progress is likely to remain as slow here as in the area of non-prescription pharmaceuticals.



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Conclusion:

What are the prospects for change?

The international and regional efforts at regulatory harmonisation reviewed in this study have much in common. Driven by a desire to improve patient access and reduce barriers to trade, the focus of these initiatives has largely been on questions that, while still intrinsically difficult, are potentially amenable to science-based agreement, such as drug efficiency, safety, and quality or best practice in manufacturing.

Results have sometimes been slow; technical capacity in many countries and the fact that different countries – with similar capabilities – take different views of the same issue, have impeded harmonisation in practice. Nonetheless, important progress has occurred around questions such as what an application for drug registration should contain.

Time and again, however, these efforts – in large part because they are focused either on the pharmaceutical industry in general or are part of even broader free-trade initiatives – do not address the wider regulatory issues facing non-prescription drugs, such as how to decide what can be sold over-the-counter or questions of sales channels and appropriate labelling. These broader matters are not only important in themselves in shaping patient access to these drugs through the pharmaceutical market. If left fragmented, they also, as highlighted in Europe – the region with the longest experience of attempting to implement harmonisation – can limit the effectiveness of such common regulations. It is hard to disagree with the assessment of David Spangler, senior vice-president at the Consumer Healthcare Products Association (CHPA) with responsibility for legal and international affairs, that in fields such as labelling and switch from prescription to OTC “there has been very little progress [on harmonisation]. I don’t think that surprises folks when you have different risk tolerances and societal differences. It is not realistic to expect things like switch approvals to be the same.”

Greater harmonisation across non-prescription drugs as a whole could undoubtedly improve the ability of patients to care for themselves and reduce needless costs to society, health systems, individuals and companies. Yet, experts interviewed for this study confirm that regulation of non-prescription medicines is not currently getting significant attention.

Broad support for greater harmonisation presupposes shared views on the appropriate role of the patient. However, as Dr Fitzgerald says, the question arises of whether “you [are] harmonising from the perspective of more rigorous regulations and control or toward freer access with greater self-care responsibility for the patient. There is no overall common understanding of what harmonisation should look like.” Mr Thomas agrees. “The question,” he says, “is harmonising up or harmonising down. A real concern that companies have is that we end up harmonising up to the highest level of distrust. Companies would like harmonisation, but only if it protects the future needs of consumers rather than reinforces the risk aversion of regulators.” Ms Darracott believes that this lack of agreement on what harmonisation should entail keeps all stakeholders reticent: “nobody is pushing for a review of the legislation. There is fear that if we open up the regulations we might lose things that we quite like. It is a ‘be-careful-what-you-wish-for’ thing.” The result, says Mr Cranz is that “certain legal provisions in the marketplace are not fully harmonised because all the stakeholders do not want more harmonisation. If that is the case, then you can’t expect anything more.” ▶

“Greater harmonisation across non-prescription drugs as a whole could undoubtedly improve the ability of patients to care for themselves and reduce needless costs to society, health systems, individuals and companies. Yet, experts interviewed for this study confirm that regulation of non-prescription medicines is not currently getting significant attention.”

Economist Intelligence Unit

Conclusion

“Until the large majority of health authorities genuinely accept that this should be the direction of travel, only change at the margins is possible. Once they do, though, the hard, practical work can begin.”

Economist Intelligence Unit

Ultimately, the issue is not one of constructing broadly acceptable legal formulae but answering the question of how much health systems and regulators are willing to trust patients and help them in providing their own self-care. Despite the rhetoric, the shift from paternalistic care to patient-centred and patient-driven care has been slow and uneven both within and between countries. Pharmaceutical regulation is only part of that bigger picture. As Mr Thomas puts it, “at the moment we have a regulatory environment founded on ensuring patient safety. This goes back to stopping snake-oil sellers in the US in the 1890s. The real challenge is how we move that regulation on to one that genuinely encourages consumer empowerment, while at the same protecting their interests. A new balance needs to be struck.” Until the large majority of health authorities genuinely accept that this should be the direction of travel, only change at the margins is possible. Once they do, though, the hard, practical work can begin.

Prerequisites for change

Any effort at regional or more extensive harmonisation of OTC regulations would require major steps towards stronger international discussion, cooperation and understanding.

Steps to define the role of consumer healthcare in the wider healthcare system: A global discussion on regulatory harmonisation in the consumer healthcare space requires key healthcare stakeholders, including patient advocates, to more clearly define the role that self-care, and within it, consumer healthcare, can play in the wider healthcare system. To what extent does consumer healthcare contribute to patient empowerment, community healthcare engagement and cost savings for squeezed healthcare budgets? What are its limits?

An international conversation on the appropriate roles of patients, pharmacists and other professionals in healthcare:

Ultimately, any harmonisation process must begin with a rough consensus on what a harmonised set of regulations should look like. This will not be possible until some broad similarity of opinion exists on the appropriate level of power patients should have in their own healthcare. Despite increasing calls for patient-centred care, this commonality of view simply does not exist, even between European countries, let alone more widely.

A discussion about the appropriate roles of culture and science:

Medicine is a scientific discipline. However, self-care frequently involves substances that may be widely held to be effective by people in certain cultures, but are met with scepticism in others. Typically, they have little formal proof to back up claims. Any multinational regulatory system will have to find ways to harmonise treatment of – or to exclude from its purview – such substances, be they traditional medicines in China and India or herbal remedies in German-speaking countries.

A focus on the specific needs of non-prescription pharmaceuticals:

Although the OTC sector has benefitted to a degree from various harmonisation initiatives centred on pharma as a whole or regional removal of non-tariff trade barriers, the range of regulatory issues and the way they interact make it difficult to foresee progress unless the OTC sector’s specific issues are addressed separately.

Efforts to reduce differences in regulatory capacity: Any system of regulations, national or regional, needs to be supervised. At the moment, even with the best will in the world, some countries could do very little to police their pharmaceutical sectors. Any harmonised system needs to help weaker regulators to improve their capacities.

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