

Thank you for giving us the opportunity to review the WHO draft Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property, A/PHI/IGWG/2/2

This document has been forwarded to the FIP Boards of Pharmaceutical Practice and Science, in order to obtain the views of these groups.

Please find the comments attached, bearing in mind that they are direct quotes from the reviewer.

We look forward to continuing our collaboration with your department. Should you have any other queries please do not hesitate to contact me.

Comments from FIP

30 Sept 2007

1. Para. 9 (1.4) c Traditional medicines. In some countries considerable work has been done to endeavour to rationalise traditional medicines (e.g. Gelfand, Zimbabwe). Provision should be made to develop this knowledge further in parallel to the research and development needs as quoted. Standards and uses of traditional medicines are very difficult to define and are usually very local in their application. Wider dissemination of knowledge about uses and possible uses should be heavily promoted to local populations.

2. Para. 20 (6.3) c Removal of tariffs and taxes
d Compulsory licensing for export (countries which manufacture medicines)

Para. 22

The plan appears to ignore adequate quality control of medicines for all three Types of diseases, whether manufactured or imported, and this includes post-market surveillance.

Years ago, there were plans for three quality control laboratories together with registration bodies in Harare, Zimbabwe; Nairobi, Kenya; and Maputo, Mozambique. I believe that only the first mentioned was actually achieved*. Regardless of this, any such laboratory and regulating body should be totally regional in its operation, and serve neighbouring countries who do not have such facilities. This immediately implies interchange of knowledge on regulating practices concerning drugs and medicines in differing countries, and negotiations to facilitate the transfer of samples between countries with ease. This requires organising special customs and transport

President
Prof. K.K. Midha
Canada
General Secretary
Mr A.J.M. Hoek
The Netherlands
Scientific Secretary
Dr V. P. Shah
USA

Professional Secretary
Prof. H.R. Manasse, Jr.
USA
Immediate Past President
Mr J. Parrot
France
Vice Presidents:
Mr J.A. Bell
Australia

Dr M. Buchmann
Switzerland
Ms B. Frøkjær
Denmark
Prof. M. Hashida
Japan
Dr M.L. Rocci
USA

Prof. M. Rowland
Great Britain
Mr P.D. Sheth
India
Mrs L.J. Stone
Great Britain
Dr Th.F.J. Tromp
The Netherlands

Chairman of the Board of Pharmaceutical Sciences
Prof. D.J.A. Crommelin
The Netherlands
Chairman of the Board of Pharmaceutical Practice
Prof. P.J. Schneider
USA

arrangements for such samples for analysis. [All this was the original intent of the three laboratories quoted.]

3. General comment. The plan is almost entirely concerned with research and development concerning new or existing drug treatments for the three Types of diseases mentioned.

Surely any such plan should give equal or even priority status to controlling disease vectors, where appropriate. This is especially important in the cases of malaria, filariases (differing types), schistosomiasis and trypanosomiasis. This need is owing to the rapidly increasing resistances shown to both the disease vectors and the causative micro-organisms by insecticides and drugs.

Perhaps therefore, in view of my comments above, the terms of reference recommended by the Working Group might be a little broader and wider in concept.

In general, we do recommend the FIP to congratulate the WHO on what appears to be an excellent, very mature document. We do hope that by implementing this strategy, research and development to counter health risks in developing countries will be significantly facilitated.

Since the daily work of many of our MEPS colleagues is to take care for the pharmaceutical aspects of medical support in military environments and/or for emergency relief and response, we are dealing with situations that may have a limited probability to occur, yet potentially devastating consequences. Therefore, the challenge of having to conduct, encourage or facilitate research and development efforts dedicated to this purpose, is very familiar to us.

From this experience, we would like to point a number of comments and remarks related to the WHO document, which are not meant to be contradictions, but rather additional information which we hope will be useful to develop the subordinate, more technical documents and to actually implement the strategy:

Overview

#	Item
1.	Develop Methodology to allocate research/development funding in order to maximise health benefits from limited resources
2.	Investigate active substances, development of which may have prematurely abandoned by profit oriented researchers
3.	Systematically use human resources from postgraduates and other junior professionals to accelerate research and development
4.	Emphasise the importance of cancer prevention, therefore intensify the collection of information regarding carcinogens in environment, drinking water and foodstuffs
5.	Intensify Crackdown on Counterfeiting of Pharmaceuticals, consider WHO-led analytical Task Force to obtain precise information

Given the scarcity of resources, precise allocation of funding to the most promising non-profit research and development efforts is imperative. Essentially the planning task is to create, with limited financial resources the largest beneficial effect possible and at the same time minimise the risk of project failures that might consume significant amounts of resources without creating a benefit at all. A systematic methodology for decision-making should be developed and should take into consideration the following factors.

- morbidity/mortality from a particular disease,
- near and mid-term future trends related to morbidity/mortality, they may be reduced by preventive action (e.g. improved access to safe drinking water), however, there may often be the risk of dramatic increase (e.g. from contagious diseases)
- availability of therapeutic options – or the lack thereof,
- near and mid-term future trends related to availability of therapeutic option, e.g., a previously unaffordable medicinal product may become substantially cheaper as soon as certain patents expire,
- future therapeutic options, such as potential Active Pharmaceutical Ingredients, the status of their development, chances/ risks of achieving/failing to achieve marketing authorisation,
- experiences from similar compounds, increasing/decreasing the probability of a successful development
- estimated costs of further developments, opportunities to cut these cost by cooperation, networking and other synergy effects.

The strategy paper points out the availability of compound libraries as an important issue to facilitate pharmaceutical research. This is a very valid point and when addressing it further, the following facts should be taken into consideration:

- the pharmaceutical industry in developed countries has access to a virtually unlimited library of compounds due to the capability of modern synthesis chemistry and high-throughput screening,
- however, as soon as the focus of development is on a particular substance, this work is extremely cost-intensive and failure to achieve marketing authorisation is perceived as a financial damage to the company
- for this reason, development is usually stopped at the earliest signs that a substance may have unfavourable properties that may result in a denial of marketing authorisation,
- however, as many of those unfavourable effects are highly dose dependent or may not even occur in a complex biological environment, chances are that this policy does result in abandoning the development of potential Active Pharmaceutical Ingredients that may have strong anti-microbiological / anti-parasitic, potentially life-saving effects

An "in-depth look" initiative, focussing at active substances, development of which had been abandoned in early stages is therefore likely to yield a number of highly beneficial substances. It has to be emphasised that prior to any clinical trial and possibly marketing authorisation, safety of the substance has to be evaluated by the same rigorous standards used by the pharmaceutical industry.

WHO's efforts to strengthen research and development for the development of medicines against diseases primarily affecting developing countries should

systematically utilise the human resources of post-graduates and other junior professionals for the following reasons amongst others:

- having recently completed their university education, postgraduates have immediate access to a broad spectrum of up-to-date scientific knowledge,
- postgraduates may be more able and willing to re-locate in the pursuit of their academic career, to improvise to overcome potential gaps and shortfalls and to innovate, finding solutions previously overlooked,
- early in their career, the ambition to produce novel scientific result (possibly as a basis for an advanced degree) may often take priority over other considerations.

WHO Draft global strategy and plan of action on public health, innovation and intellectual property identifies cancer as a Type I disease that does affect both developed and developing countries and which prevalence is significantly increasing in developing countries. As the global research and development effort to find new therapies against cancer is already very intense (and at the same time, very intensive in its use of technological, financial and human resources, additional initiatives to strengthen that branch of research in developing countries may be less likely to produce results unless they systematically address gaps that may currently be overlooked by the global research and development efforts.

However, the key to reducing morbidity and mortality from cancer, in particular in developing countries, is prevention. To improve prevention, the following steps should be useful:

- continue to implement WHO's anti-tobacco initiatives
- gather and compile comprehensive information on the presence of known carcinogens in the environment, in drinking water and foodstuffs,
- a lot of information on the above-mentioned issue may already have been acquired by government or NGO initiatives – a WHO-led network may be useful to compile this information, avoid duplication of effort
- based upon information governments and industries should be called upon for corrective/preventive action aimed at significantly reducing human exposure against carcinogens, addressing the most significant sources first.

Counterfeiting has accurately been described as a major risk to health in developing countries. Strategies to reduce counterfeiting may include the following steps:

- strengthen WHO's IM-PACT¹ efforts
- set-up a WHO-controlled laboratory capability, allowing the state-of-the-art of pharmaceuticals in those regions most affected by drug counterfeiting,
- systematically use the advances in analytical chemistry such as more affordable GC- or HPLC units, better separation techniques, reduced solvent consumption, lighter, readily deployable equipment etc. in order to obtain sufficient data even in member states where they previously been unavailable
- set up laboratories in strategically convenient duty stations, taking into account population density, consumption of pharmaceuticals, location of pharmaceutical production facilities and accessibility; so collected data may

¹ IM-PACT = International Medical Products Anti-Counterfeiting Taskforce

represent as closely as possible the current state of production and availability of pharmaceuticals in developing countries,

- use pattern of impurities and other quality deficiencies to trace back, if possible counterfeited products to their originator,
- implement quality assurance policies such ISO 17025 to enhance credibility of laboratory results
- collect and analyse epidemiological data for health risks likely to originate from counterfeited products, e.g.
- antibiotics containing only a fraction of the declared dose may have accelerated the development of resistant strains,
- "antimalarials" containing placebo only are likely to result in increased morbidity/mortality from malaria
- use the collected information to build up, strengthen and sustain the political will to crack down on the counterfeiting of pharmaceuticals in the affected member states.

1. Section 3.4 of the annex, page 7. a) "develop and promote traditional medicine within an evidence-based framework." That sounds nice, but in reality is probably the wrong way to go. In order to gain evidence of effectiveness, large, properly conducted clinical trials would have to be conducted. These are costly and time consuming and unless there is some overwhelming reason to expect pharmacologic activity, this seems like a waste of funds.

This might be said for traditional medicines that might be intended for diseases where no adequate medicines presently exist. That would at least make more sense.

2. Section 6.2, e of annex on page 10 "Minimize the public health consequences of counterfeit and substandard drugs" While it is difficult to argue with that statement, an approach that is more direct and aimed at production and distribution of counterfeit and substandard drugs would be more efficient and more practical.

Efforts should be made to stop/prevention the production of these products as well as their distribution.

A multi-phase endeavor is needed; with practitioner awareness, better policing and inspections/surveillance, campaigns against corruption of inspectors and regulators, closing vulnerable spots in the distribution channels and employing anti-counterfeiting technologies.

Overall the impression is that the policy, while ambitious, is quite comprehensive and covers most issues. There are some aspects from a public health perspective and from an application perspective that raise questions on the process of this review. It is a very aspirational policy and will be difficult to encourage governments to incorporate all aspects of this policy into national health, but it is no bad thing to set standards high. It may be difficult for much to translate into action, certainly in the short term.

Issues around policy application

As described this is a very aspirational policy and some of the language used is open to interpretation to suit a specific stakeholders needs. It may be worth revising some of the broad specific actions within the policy to set specific targets, especially for developed

countries in terms of financial and other commitments where relevant to the policy element. This would also enable Progress indicators to be more specific as well. For example in Element 2. Promoting research and development which currently contains the following information:

Element and sub-element: 2.1 Increase funding for research and development that focuses on the health needs of developing countries

Specific actions (a) Developed countries to devote a larger proportion of their health research and development budgets to the health needs of developing countries

Stakeholders: Governments of developed countries; development partners

Time Frame: 2009–2015

Progress indicators (i) Percentage increase in health research and development budget of developed countries devoted to health needs of developing countries

In this case the specific action could suggest or recommend an aspirational proportion of GDP that developed countries should devote this. This group does not have the expertise to recommend specific targets but this would provide countries with a much clearer indication of what is expected of them from the global community and for their own citizens to determine how successful their governments are at meeting international commitments or obligations.

Public health issues

Some apparent omissions from a public health perspective that were identified were:

All countries should be encouraged to develop chronic disease surveillance systems – not only does this allow you to measure the effectiveness of national initiatives, but also to identify early any emerging health challenges. This should be explicitly stated in the research development section, you cannot have just product development because it does not encourage good implementation practices.

In the section on recruitment and training of health professionals- this also needs to be addressed from the perspective of 'poachers' , those developed countries such as Australia who rely on professionals trained in developing countries. You do not want to stem individual opportunities, but do beneficiaries of foreign skill development owe a debt (either monetary or in-kind assistance) to the country which invested in this skill. ESPECIALLY IMPORTANT – the document does not at any point mention that national/regional consumer advocacy bodies should have a stakeholder role in the development of this agenda.