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**Introduction**

This report discusses the protective measures that would be needed to ensure that the objectives of the Health Impact Fund (HIF) are met. It suggests many measures for this and cautions against unrealistic assumptions and expectations. Given the lack of data and infrastructure availability in many developing countries, this paper suggests that the HIF should not stretch its resources too thinly, should have a clear focus and should prioritize diseases and treatments/drugs which would be eligible under the HIF. The protective measures suggested include independent assessment of utilization of funds by pharmaceutical companies and government entities, and framing guidelines for marketing. Regarding issues of efficacy, the article suggests that the HIF will have to approach this on a case-by-case basis and should consider the overall health status of the population in assessing efficacy. It argues that ethical dilemmas cannot be wished away by the HIF and that combining ethics with principles of economic rationale will be a challenge for the HIF.

**Section I**

The objectives of the HIF are:

1) Incentivize development of drugs for neglected and Type II diseases through an Impact Fund System.
2) Ensure the accessibility and availability of drugs registered with the Fund.

In this paper, by ‘protective measures’ we mean measures that would enhance the effectiveness of the HIF and ensure that funds under the HIF are allocated to those registered with the HIF in a transparent, and rule based manner, and that the HIF is protected from measures like unnecessary promotion and sale of drugs registered with the HIF. In this paper some such measures are listed and examined but this is not an exhaustive list of protective measures. The paper by Aidan Hollis, *The Health Impact Fund and Price Discrimination* discusses some of the points raised in this paper.¹ To avoid repeating those arguments/points it is presumed that readers are familiar with the paper.

Universal access to health care and drugs is not available in many countries. The cost of medicine is an important factor in determining access.² In many countries the cost of medicines forms a significant portion of the health care budget, and for individuals with no insurance coverage or access to provisioning of drugs by governments it may amount to an additional burden. In terms of market size, the global market is a skewed one with

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¹ Aidan Hollis (2009), *The Health Impact Fund and Price Discrimination* [www.healthimpactfund.org](http://www.healthimpactfund.org)
the top ten pharmaceutical firms accounting for about 50% of global sales, while nine OECD countries account for about 80% of global pharmaceutical sales. The largest market is USA with 45% of the global share, but Japan at number two in terms of market share accounts for 9% of global sales. The market share or revenue of pharmaceutical companies do not however tell us much about the health condition of the people; rather they reflect the economic power of the pharmaceutical industry and the structural imbalances between cost, access and the health condition of the population. This skewed nature is further corroborated by the fact that generic medicines account for 14% of the market in terms of value, although in many markets they represent about 40% or more in terms of products. \(^3\) It is not just the price differential that makes the difference; the variation begins at the level of ex-manufacturer price.

Another factor that complicates access is insurance schemes and their coverage. Many insurance schemes have a co-pay requirement and also set limits to the costs of drugs and treatments. In the Netherlands, where employees have to be compulsorily covered by insurance, out-of-pocket spending is hardly 6%, while public health care programs provide 5% of the health budget. The share of drug costs in the total health care budget was a modest 12% in 2000. \(^4\)

The stark reality is that the twin problems of availability and access are not only related but also influence each other. Just ten therapeutic classes of drugs accounted for 36% of global sales in 2006. And most of the blockbuster drugs are not for neglected or Type II/III diseases. The 10/90 problem is too well known to be discussed here. In this context if the HIF is to make a difference it has to ensure that the issue of affordability is addressed adequately, and the utilization of the HIF should be explicitly linked with finding a solution to this problem. At the same time it is also important that resources under the HIF are put to the best use; the drugs/medicines made available under the HIF should have significant efficacy, and their health impact could be assessed and verified and the outflow from the Fund linked both with efficacy in terms of individual health and overall health impact. But this is a daunting task and the HIF has to consider some measures to ensure this. In this report we use the term ‘protective measures’ with two objectives: measures which ensure that the objectives of the HIF are met in the best manner, and measures to ensure that there are no leakages, over-estimation or wastage of funds and medicines made available under the HIF.

At this juncture the working structure of the HIF is not clear and neither are the mechanisms which the HIF would rely upon or use in various countries for implementation, monitoring and assessment. This paper assumes that the HIF has a working structure and does not take into account the proposed regional variations, but takes the HIF as a global fund with a global focus.

Countries have used different strategies and policies in tackling the issue of affordability. Drugs and medicines have no substitutes and states do not meet all the health needs of the

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\(^3\) OECD (2008), *Pharmaceutical Pricing in a Global Market.*

population, except in countries like Cuba. The sheer heterogeneity in price regulations indicates that countries use a variety of policies, and often more than one, to regulate prices. According to the literature there are eleven major categories of regulation:

1) **Global budgets:** The maximum annual spending limit for pharmaceutical products is fixed - the limits can be for geographical regions or for classes of drugs or individual products/drugs. The HIF can fix an annual spending limit for a drug for a region/country, in terms of quantity or reimbursement or both.

2) **Prescribing budget:** Prescription limits are set for physicians and overruns are not routinely permitted. Limits for prescribing the drugs can be set, based on the need for the drugs and their availability.

3) **Profit control:** The regulator fixes the maximum annual limit for profit growth. In the HIF this can be done to ensure that the manufacturer or patent holders do not ‘make a killing’ from the HIF.

4) **External reference price based price control:** The price or maximum reimbursement level for patented medicines is fixed on the basis of price(s) for similar drugs elsewhere. The reference country/countries and products may vary over a period of time. The HIF can use the price of generics or therapeutically equivalent products as the reference for fixing the price.

5) **Price control through negotiation:** The regulator sets the prices using negotiations with prices are in different categories such as maximum price, cost plus formula, price freeze or limits for increase etc. The regulator being a major or bulk buyer can leverage that to bargain for cheap prices and differential pricing for government sponsored schemes and hospitals. Private foundations also use similar strategies to buy in bulk with reduced prices. In such negotiations the price elsewhere is also considered and the threat of allowing parallel import is used to bring down prices. This method has many merits but its effectiveness is marred by the leakages in the system and the mismatch between supplies negotiated for and the actual needs of the patients. A major problem with this method is that in the absence of estimates about cost, it is difficult to negotiate for a price that is reasonable, and prices elsewhere can at best be taken as indications because in markets there are different types of prices for different categories of customers. Still, this method is widely used as it is easy to implement and the budgetary limits and the negotiated prices can be linked to ensure that the set limits are not exceeded. But when the regulator is not well informed about costs and prices and when the number of suppliers is limited this method may not be the best solution. As discussed elsewhere such a negotiated price control will be necessary when the manufacturer or patent holder is unwilling to produce in enough quantities on account of low profit margins or returns not commensurate with the investments made. When the government tries to suppress the prices through price controls, the HIF can ensure that a part of the loss on account of price control is made good through reimbursement from the HIF.
6) **Generic reference pricing:** The reference price above which consumers will not be reimbursed is set on the basis of prices of similar products with similar/almost similar efficacy within the country. This is done in the case of generic drugs. For generic producers this pricing indicates the maximum price they can quote when they apply for supplying medicines. Since consumers know the reference price they can opt for drugs that are at par or below that price. This works well when there are many generic producers and there is no cartel of generic producers. For those producers who can afford to reduce prices and offset that loss through increase in volume, the reference prices are very useful. This will be useful for the HIF when there are many generic producers and among generics there is a significant price difference. The HIF can encourage low cost and good quality generics by fixing their price as the reference price.

7) **Therapeutic reference pricing:** Both generic products and patented products are subjected to reference pricing. For patented products also the generics may be taken as a base for reference pricing. In some markets where generics are available, but patented ones are preferred because of brand loyalty, preference by physicians and other factors, the HIF can use this method and thereby encourage the use of generics.

8) **Pricing based on evaluation:** Economic evaluation or Cost-Benefit Analysis is used in deciding the eligibility of a product/drug under insurance or provision by government. The level of reimbursement can be set and the co-pay or cost borne by the consumer is also set. Thus 80% of the cost may be covered by insurance while 20% has to be borne by the consumer or by a third party (e.g. employer). The evaluation or cost-benefit analysis although controversial brings in rational decision making and constrains the tendency to over-prescribe medicine and unnecessary treatments or treatments with little benefit. The flip side is that such analysis is often contested as there are methodological issues in estimating costs and benefits, and those who need the treatments most may be affected in the process because they may be solely dependent on insurance or schemes like Medicaid or public sector services like the NHS. This method is discussed elsewhere in this paper.

9) **Generic substitution:** Unless patented medicine is prescribed as the only acceptable medicine, use of generics by hospitals and health care providers is permitted. Usually the regulator provides guidance on prices of generics and the list of permitted generics. This will be relevant for the HIF particularly when there are many generics and the patented medicine is only one of the options. The HIF will have to prepare the list of approved generics and their respective prices for claim purposes.

10) **Incentives for prescribing generics:** Doctors or health care providers are given incentives for prescribing generics. This method, although undertaken with the intention of limiting budgetary outflow and encouraging generics, raises some ethical issues. Generics may be prescribed in more than the quantity necessary as
an incentive is linked to prescribing generics which may result in unnecessary use of drugs. So this has to be linked with ethical guidelines and guidelines on prescriptions to ensure that the system is effective. The HIF can use this and can give incentives subject to rules on marketing of drugs. The HIF will have set limits for such incentives and promote rational use of generics rather than over-use and medically unnecessary consumption.

11) **Digressive fee structure:** The margin receivable by the pharmacist is fixed and the higher the cost, the lower is the margin the pharmacist is entitled to. This is done to encourage cheap/generic drugs to replace expensive/patented drugs. But this will not work when the pharmacist relies less on this as a source of income. The relevance of this for the HIF is not clear because the HIF may not use this method. Since the HIF is not likely to deal with distributors or sellers directly this method is of very limited relevance.

In reality pharmaceutical markets are not uniform across countries or within countries. So governments and regulators use more than one method and change the mix of the policies. But regulations do have an impact and increase affordability. On the other hand governments can also intervene in the market through other means and put a check on prices. For example drug production in the public sector can be encouraged and for critical medicines like vaccines government can be the sole producer or sole buyer and thereby contain the prices. Other options include encouraging cross-border trade, allowing parallel imports, or using the Doha Declaration Paragraph 6 to issue compulsory licensing for export to the country. But this solution has been of limited use and not many countries have used this for enhancing accessibility to drugs for HIV/AIDS.

According to the Rand study;

“For example if the United States implemented price controls and negotiations similar to those found in other developed countries, then U.S revenues would fall by as much as 20.3 percent. Finally the results show that the impact of regulations on revenues increases over time”.

The study by the International Trade Administration for the U.S. Department of Commerce comes to similar conclusions and argues that price suppression reduces

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5 See for example the following studies on France and Norway: Nathalie Grandfils (2006), *Drug price setting and regulation in France*, IRDES (Institut de recherche et documentation en économie de la santé); Dag Morten Dalen (2006), *Steinar Strøm Tonje Haabeth*, Health Economics Research Programme at the University of Oslo.

6 For an analysis see Vanessa Bradford Kerry, Kelley Lee (2007), “TRIPS, the Doha declaration and paragraph 6 decision: what are the remaining steps for protecting access to medicines?”, *Globalization and Health* 3:3.

7 Neeraj Sood et.al (2008) “The Effect of Regulation on Pharmaceutical Revenues Experience in Nineteen Countries”, *Health Affairs*, Published online 16 Dec 2008, [http://content.healthaffairs.org/cgi/content/abstract/hlthaff.28.1.w125v1](http://content.healthaffairs.org/cgi/content/abstract/hlthaff.28.1.w125v1)

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The Health Impact Fund and Protective Measures: RIS 6
the revenue from patented drugs and thus affects the investment for R&D for new drugs.\(^8\)

One conclusion that is obvious from these studies is that price controls enhance affordability for consumers and have become part of public policy in many countries, including OECD countries. Some countries try to combine price controls with assessment of the efficacy of the drug and its cost effectiveness.

While these studies are important their limitations are obvious. These studies have studied the price regulation issues in OECD countries. Although some studies on drug price regulation and control in developing nations have been done, there does not seem to be a comparative study on drug price regulation in developing countries and the impacts of such regulation in enhancing access. However from the studies cited and from the literature one can conclude that price controls and price regulations enhance affordability. Other factors like availability of generics and health insurance have a significant impact on the affordability of drugs.

Still, caution is required in introducing restrictions that will have overall negative impact although they may meet some immediate objective like savings on account of enforcing co-payment. According to one commentator;

“Restricting access to drugs through excessive co-payments or quantity controls or through inflexible therapeutic substitution policies without regard to specific circumstances cannot be expected to produce good results for patients or budgets, and is often “penny wise and pound foolish.” Most studies find that traditional drug formulary management and drug utilization policies designed to curb drug expenditures boomerang. Inappropriate drug cost-sharing and utilization reviews designed to control drug expenditures result in unintended consequences, including suboptimal use of medication; health status declines; or increased use of more costly ambulatory or institutional care.”\(^9\)

In the context of the HIF it can be surmised that regulation will enhance the effectiveness of the HIF in increasing access and enhancing affordability. Since the HIF is a reward mechanism that is based on performance and efficacy, using the regulatory framework should be the priority of the management of the Fund when the HIF is put into practice. Obviously the HIF can be used to negotiate reductions in price when effectiveness is established and there are enough suppliers. Its effectiveness can be increased by harmonizing the HIF with regulatory systems for pricing and provisioning where it is possible to do so. But in countries where the system is weak or largely non-existent and where the market is the arbiter in pricing

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issues the HIF will have to consider a mechanism that ensures both access and affordability. For example the HIF can use public sector hospitals and other not-for-profit service providers to increase access and affordability even as the drugs are sold in the open market or through pharmaceutical stores at fixed prices. But in such cases leakages or diversion from public sector hospitals to market can be a problem. This can be partly solved by giving different colors for tablets and using different packing for different customers. But as the examples below indicate, the ground reality is complex and there are any number of methods to control price and access to drugs.

The combination of market, insurance schemes, provision by governments and the consumer bearing a part of the burden is done in many ways. As countries experiment with many methods and learn from the experiences, they modify the measures and bring in new schemes. The interface between competition policy and drug regulation may not be direct but competition policy can be used to ensure that there are no cartels and producers do not collude with each other to defraud the consumers and government. Although using measures like compulsory licensing can enhance affordability and induce competition we do not discuss that in detail here as much has been written on this elsewhere.

In the case of China the policy has undergone many changes, and while the state is keen to control the prices of some medicines it is willing to allow the market to set the price in some categories. The National Development and Reform Commission (NRC) sets the maximum price for drugs in an essential drug list, special drugs used in family planning, vaccines and for drugs whose distribution and use are restricted (e.g. medicines for psychological disorders; narcotics used in treatments). The maximum retail prices are set based on the average cost of production. For all other drugs, the prices are determined by the market. The government is a procurer in bulk and the prices are decided on the basis of bidding. The government has opted for a three tiered pricing policy for patented drugs, branded generics and general generics. But the shortcomings of the pricing mechanism are as follows:
1) As quantity is not restricted this will not result in control over health spending growth,
2) Low priced products ‘disappear’ from the market,
3) Manufacturers stop producing drugs for which margins are low.

The lack of co-ordination between the drug regulatory authority and the pricing authority has also been cited as another weakness of the system. In short, the Chinese system which combines government control through price fixing for some categories and market mechanism for others is effective although there are problems or shortcomings.10

India is a country that has a long experience with regulating prices of drugs and where affordability is a major issue. According to a survey, in non-institutional treatment 80% of the cost of treatment is spent on medicines. Various studies including the one by the National Commission on Macro Economics and Health have highlighted the nexus

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between poverty and access to health/drugs. The poor are more likely to fall sick and are less likely to be able to afford treatment/drugs. As medical treatment costs escalate, the poor who cannot afford this are pushed below the poverty line or are forced to borrow at exorbitant rates of interests. As India has universal health insurance, the poor have to rely on the public sector hospitals. India experimented with price controls in 1962. In 1970 the Drug Prices Control Order was issued. It has since been revised many times. Under DPCO the retail prices are fixed for drugs covered under the Order. Over the years the number of drugs has come down from 347 in 1979 to 74 in 2008. The market share has also come down from 80% to 20%. The market share however is not the best indicator because there are so many formulations and combinations in the market in India and of these many have little therapeutic value. The National Pharmaceutical Pricing Authority (NPPA) has powers to determine overcharging and recover amounts overcharged, enforce the DPCO, monitor prices of Non-Scheduled drugs and fix the prices of APIs under schedule and their formulations.¹¹

Thus although the NPPA has the authority and there is a mechanism for bulk purchase through tenders/pooled procurement, affordability is a critical issue because of factors like poverty, imperfect competition in the market, and a lack of universal health care or universal health insurance. Although India has a dynamic generics industry and a well diversified pharmaceutical industry, affordability is a major issue. With the growth of private insurance and private medical care institutions, affordability will continue to be a major issue. The lessons from India’s experience with the DPCO are relevant for many developing countries. The DPCO succeeded because the generics industry could compete with MNCs and supply drugs at cheaper prices. Besides this the market size was an inducement for more investment and benefits from economies of scale could be reaped. As the DPCO and drug regulation was for the whole country, manufacturers and distributors, there was no confusion over the regulatory system. On the other hand issues like spurious drugs, and the flooding of the market with formulations/combinations that are of little therapeutic value remain challenges for regulators.

*The Task Force to Explore Options other than Price Control for Achieving the Objective of Making Available Life-saving Drugs at Reasonable Prices* headed by Pronab Sen made many recommendations to increase the affordability of drugs.¹² One of the recommendations was to reduce/eliminate taxes and tariffs including octoroi and custom duties and pass on the benefit to consumers. Many of its recommendations would be relevant for developing countries where affordability is an issue. The HIF can draw some points on increasing affordability from this report.

Studies have found that generics are generally cheaper and that intervention by the government in the form of reference pricing and price controls is effective in reducing

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¹² *Task Force to Explore Options other than Price Control for Achieving the Objective of Making Available Life-saving Drugs at Reasonable Prices*, September 20, 2005, Submitted to the Department of Chemicals & Petrochemicals, Government of India. See also the *Policy Brief on Draft Pharmaceutical Policy 2006* [http://www.clraindia.org/include/Pbrief1.pdf](http://www.clraindia.org/include/Pbrief1.pdf)
prices. The subsidization of medicines is done by many governments, and in some countries like Australia consumers make a co-payment. Australia’s Pharmaceutical Benefit Scheme subsidizes drugs, and according to one estimate, in 1998/99 139 million prescriptions were subsidized at a cost of $3 billion. In the UK it has been reported that in 2003 the share of generics prescribed under the NHS was 73%, accounting for about 24% of the expenditure.

According to a study by OECD, variance in per person spending on pharmaceuticals is significant. The USA had the highest level of per capita expenditure at $792 PPP while Mexico had the lowest at $144 PPP. It also shows that pharmaceutical demand is relatively income inelastic. The study makes many interesting observations but it is difficult to agree with some of the findings and suggestions. For example it argues that wide spread insurance coverage distorts the market for pharmaceuticals and that consumption would have been less had there been no insurance or were consumers to bear the cost.

The HIF should consider the various public policy options and should include price controls in its tool box. Since the HIF is primarily oriented to encourage innovation for enhancing accessibility and affordability, the thinking has to go beyond the market and should focus on making the best use of the HIF in terms of health outcomes. Subsidies by governments and insurance coverage might result in excessive consumption and unnecessary prescriptions but the overall benefits should be taken into account in evaluating them. The HIF cannot afford to ignore the possibility of unwanted consumption and unnecessary prescriptions but these can be restricted by taking protective measures. For example, limits on rewards and numbers of prescriptions can be fixed. In the case of vaccines it is easy to estimate the demand or required quantity and restrict reward to that extent. The HIF can convince the insurers to extend the coverage to the drug registered with the HIF and the insurer can set limits of reimbursement for each drug for each consumer. The challenge lies in extending availability and affordability in countries where there are no insurance schemes or universal health coverage by the public sector. The HIF can use various studies on pharmaceutical pricing and regulation and list the potential issues that need to be addressed by formulating protective measures.

To sum up, governments intervene in enhancing affordability in many ways, and however insufficient it may be it does have an impact on affordability. But as health budgets increase due to increased drug prices, governments find it difficult to increase subsidies and other forms of support. But in many countries the governments allow the market to fix the price for most drugs while selected drugs are brought under some form of price control. Although there can be huge price differentials between neighboring countries, cross-border trade in pharmaceuticals is not significant.

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14 US Federal Register Notice: Drug Pricing Study available at 
In many developing countries and LDCs the lack of a home grown and innovative generics industry hampers effective intervention in enhancing affordability. Although there are many generic producers who are willing to supply at cheaper prices in these markets, the price variation among countries is significant. Governments can negotiate and reduce the prices as they buy in bulk but there are many constraints in using this method. The budgets for drugs are limited and the governments have to prioritize drugs that are essential against drugs that are not that critical. In the case of patented drugs for which generics are not available, the dilemma is acute. Donations and philanthropic efforts in providing drugs are necessary, but not sufficient to solve this problem.

### Section II

From the perspective of the HIF, protective measures are necessary to ensure that affordability and access are linked. Some such measures are:

1) Fixing the maximum price for the drug for the whole country and ensuring that this is adhered to.
2) Encouraging the local generics industry to produce drugs in the desired quantities. This may involve the import of APIs where they cannot be produced locally. In such cases the HIF has to ensure that APIs are made available at reasonable prices
3) Since the drug eligible for reward from the HIF is likely to be made available from different sources, the manufacturers and the sellers have to be sensitized about the objectives of the HIF, and their co-operation is vital in ensuring affordability.
4) Where there are spurious drugs, vigilance is required to ensure that spurious drugs are not sold for the drug under the scheme. This would necessitate applying drug regulations against spurious drugs for this drug. Since spurious drugs can do harm and destroy the credibility of the drug registered under the HIF, the HIF has to assess the nature and magnitude of the problem of spurious drugs before introducing the drug in the market. With the help of the government the possible sources of spurious drugs have to be identified and steps should be taken to tackle this menace. For this it may be necessary to do post-marketing surveillance, sample collection and to monitor the availability of the drug, as well as educating the consumers against using spurious drugs.
5) The difference between the market price and the price under which it is made available by the public sector should not be high. If the price difference is high diversion is likely to happen.
6) Assessing the overall demand and supply of the drug registered under the HIF. To increase the quantum of reward available from the HIF the manufacturer may indulge in over-selling and over-promotion of the drug. Sales figures may be inflated and manufacturers and distributors may collude to inflate the figures. The HIF has to rely on government and other parties to undertake post-market surveillance and verify the data provided by the manufacturer in such cases.
7) Penalties and fines should be imposed for falsification of data and for making claims not commensurate with production and consumption.

8) The HIF has to make a realistic assessment of the impacts of the drugs and the quantity needed in the country before allowing the registered drug to be sold widely. Based on this the HIF can fix the country limits for quantity to be sold, or quantum of reward, or both, in the initial stage itself. This can be revised later, but it is essential that the HIF is clear about the size of the market for the drug, the revenue from the drug and the quantum of the reward that is payable.

9) If the drug is subsidized by the government or public sector, the quantum of the subsidy should be taken into account in arriving at the reward. While such subsidization will increase affordability it is equally important to ensure that such subsidization does not result in overuse of the drug or its prescription in cases where it is not required.

Section III

Although studies on cost effectiveness of drugs are not uncommon, this is a controversial issue. While methodology is often a matter of contention, the heterogeneous nature of the global pharmaceutical market and the wide disparities in consumption and production, on prices and access and regulation make it difficult to extrapolate results. Another constraint is the availability of reliable data. According to one commentator:

“Although I acknowledge there is no single answer to the question of the right cost figure to use, I indicate that deciding which conceptual setting matches the decision in question is often not easy and often made incorrectly. Some consequences of using the conceptually correct methods may raise some difficult political questions, but those questions will yield better answers if there is agreement in advance on what framework and measures to use and how decisions are to be based on this information.”

At least ten countries use one form of economic evaluation or another to assess cost-effectiveness, or to decide on the quantum of reimbursement or guidance on health technologies. Mark Hammond has analyzed the experience in these countries and has put forth lessons from these. In my opinion the lessons he has pointed out would be relevant for the HIF if it were to opt for a Cost-Benefit Analysis or economic evaluation.

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The more medicine is sold, the more the health impact will be and so the more will be the reward. This logic sounds well but is deceptively simple. Health impact is based on estimated QALYs / DALYs, but arriving at this is difficult in the absence of reliable disease burden data and other data on public health, including epidemiological data. Another issue is in estimating impact factors such as famines, natural hazards, epidemics, and diseases that abnormally affect mortality. These have to be taken into account lest there should be an over-estimation of the impact and an under-estimation of factors that adversely affect the health of the population. To give an example, while a neglected disease may be afflicting a huge population, say twenty million in a country, it is likely that of that twenty million, 10% or 15% may also be suffering from chronic malnutrition, or, due to the impact of high IMR/MMR (Infant Mortality Rate/Maternal Mortality Rate) the effectiveness of the new drug may be less than had been anticipated. According to a study:

“In conclusion, we find that although some periods of time are likely to result in more productive discoveries than others, there is no evidence that gains from pharmaceutical discovery have been fully realized. To the contrary, it is likely that as valuable new pharmaceutical products are introduced, and drugs made more accessible to broader populations, further improvements in life expectancies will result”17

While it is true that the HIF is not a panacea and its focus is on select diseases, it is essential that impact of the new drug and the HIF in terms of health outcomes does not get distorted on account of factors that are beyond the control of the HIF or producers of drugs. Hence we suggest that as a protective measure the HIF should evolve a methodology to estimate the impact of the new drug, taking into account the disease burden, mortality rates on account of various diseases/causes, and the interplay between diseases and treatments in enhancing/diminishing health outcomes.

For example, a vaccine is not a cure for malnutrition but it can enhance the chances of survival of a child and thereby enable better health outcomes from other treatments/drugs. In some contexts where there is an huge overlap of women and children suffering from a disease and also with poor survival rates on account of IMR/MMR, in order to enhance the effectiveness of the new drug and its health impact, the HIF can work with others to attack twin problems simultaneously – reduce IMR/MMR and enhance health outcomes and survival with the new drug. Although reduction in IMR/MMR may not be the focus of the HIF, drugs may be ineffective when other causes diminish the prospects for survival. Thus managers of the HIF should take a holistic perspective in evaluating the QALYs and DALYs and assessing the costs and impacts.

There are inter-generational and intra-generational equity issues in health and disease issues. These cannot be wished away but they should not result in paralysis, and

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dilemmas and bio-ethical issues should not over-shadow other issues. For example in estimating the health impact of two drugs, it is possible that one drug that saves the lives of young children benefits that generation, whereas a drug that increases the longevity of persons who are suffering or prone to diseases that afflict adults most benefits the contemporary generation(s) of children. With limited funding which one should be given priority? What are the QALYs and DALYs in each case, and are QALYs and DALYs alone sufficient to assess the health impact when two such drugs are eligible for consideration under the HIF? This example is just illustrative, but different diseases have different health impacts and often such impacts influence each other, so the HIF has to develop reliable and acceptable methodologies to assess outcomes and impacts in countries.

The case of NICE has been discussed by the Innova-P2 group in the paper circulated at the Beijing Workshop (August 2009), so the points raised therein are not discussed here. However there are many issues that need to be considered before using NICE as a model. First of all, in most developing countries there is no equivalent to NICE. Although drug regulation and drug pricing mechanisms are in place there are no bodies that perform the function that NICE does. The NHS in the UK is an exception. NICE relies on studies done by others, has developed methodologies to evaluate drugs and treatments and thus is capable of doing a meta-analysis and arriving at a conclusion, however controversial it may be, which can be defended on scientific grounds. But duplicating this in a developing country or LDC context is expensive and more than the costs, the major limitation will be lack of studies and lack of human resources to perform such an analysis. Another issue is that in the case of drugs for neglected diseases and Type II diseases, making an analysis such as NICE does will be premature when the drug has not been widely used. Instead the HIF should focus on the clinical efficacy of the drug under the HIF and its potential impact. It is assumed that there are no substitutes or equivalents for the drugs introduced under the HIF and hence the HIF supports them by rewarding them.

The HIF can study the methodologies developed by NICE and its philosophy of evidence based policy making and informed decisions on supporting treatments/drugs. This will enhance the credibility of the HIF besides bringing in rigor in the initial stages itself. Such an approach will indicate to the governments and other funders that the HIF adopts a scientific approach and is capable of analyzing data submitted on efficacy and health impacts.

The HIF can make use of publications like the International Society for Pharmacoeconomics and Outcomes Research report, Good Research Practices for Measuring Drug Costs in Cost Effectiveness Analyses: A Report of the ISPOR Drug Cost

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18 See also Michael Schlander (2007), *Health Technology Assessments by the National Institute for Health and Clinical Excellence A Qualitative Study*, New York: Springer.
19 In the case of cancer, although NICE recommended against a particular drug, patients objected to its discontinuance from treatments covered under the schemes because they found that it was effective in treating lung cancer. The recent controversy over NICE’s decision on the breast cancer drug Tyverb produced by Glaxo is another example.
The Health Impact Fund and Protective Measures: RIS

Task Force \(^{20}\) and form a group to assess the methodologies of bodies performing cost-effectiveness analysis and develop a set of best practices/guidelines for evaluating drugs under the HIF.

To conclude, measuring cost-effectiveness and doing a cost-benefit analysis will be a challenging task for the HIF. Although there have been discussions on QALYs and DALYs in the literature on the HIF this aspect has not yet been given much attention. Still, it is necessary that the management of the HIF is aware of this and develops a methodology to undertake this exercise.

Section IV

It will be in the interests of the producer to market the drug as widely as possible and increase sales. However it is essential that ethical practices are followed by the producers and distributors when marketing the drug. At the global level there are three codes; International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) code, the World Health Organization (WHO) guidelines, and the European Federation of Pharmaceutical Industries and Associations (EFPIA). Besides these there are many self-regulatory codes on advertising, promotion, providing samples of drugs as gifts, direct selling to consumers, claims made in the publicity material etc. \(^{21}\) In some countries the self-regulation codes are supplemented by guidelines issued by the regulatory authority. Thus although there is no guideline/code that is put into practice in all countries, there are key elements in different codes and from them it is easy to synthesize a set of guidelines or best practices. This should be in addition to the regulation imposed by regulatory authorities. (See the table at the end of the paper).

The issue of permitting direct to consumer advertising of prescription drugs will have to be considered by the HIF in developing its ethical code/guidelines. According to one commentator;

> “Given the likelihood that research will find both substantial costs and benefits to DTCA of prescription drugs, policy strategies should be sufficiently nuanced to target wasteful demand creation while preserving public health benefits.” \(^{22}\)

\(^{20}\) www.ispor.org

\(^{21}\) For a list of these see Judith Grice (2008), Global Pharmaceutical Marketing: A Practical Guide to Codes and Compliance, London: Pharmaceutical Press.

The legal dimension is important and that itself would need another paper. The interface between law, regulation and pricing is important but too complex to be discussed here. In this it is better to refer to law and practice in each country and develop guidelines. For an example of case law and regulation of drugs in the UK see Gordon E Appelbe, Joy Wingfield (2009), Dale and Appelbe’s Pharmacy Law and Ethics, London: Pharmaceutical Press.

This study is based on the experience in the USA, and the situation in other countries may not be the same because the influence of media, access to media and channels of communication are different. If the HIF were to support direct to consumer advertising of prescription drugs it should link that with the overall guidelines and should consider ethical issues in prescribing and regulation of prescription drug promotion. It should be pointed out that in such issues there is enough scope for ambiguous rules and rules that conflict with one another. Since some issues are cross-cutting issues the HIF should develop an approach that is feasible, ethically appropriate and relevant for fulfilling the objectives. Similarly in health communication also there are issues that need to be debated. Communications about the drug should not give a misleading impression and consumers should be made aware of the actual use for the drug and be cautioned about side-effects, effects of over-dosage etc. Moreover it is also necessary to consider codes already in practice, and whether they are voluntary or not, before framing one by the HIF. In this, the HIF can benefit immensely from studies done in health communication, particularly on ethical issues in communicating about drugs and vaccines. A well-designed framework in this area can function as a protective measure.

In this paper I have sketched an outline of major issues in designing protective measures for the HIF. These need to be developed further and discussed. In my view the HIF can start working on protective measures and debate the issues in order to evolve a set of measures so that the HIF as a concept and practical plan which is well-developed and ready to be implemented.

### 5.5 Overview of control: regulation or self-regulation

**Table 5.1 Summary of control mechanisms by country**

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<tbody>
<tr>
<td>Australia</td>
<td>TGA</td>
<td>No</td>
<td>Yes</td>
<td>Self-regulation</td>
<td>IAMA</td>
<td>IAMA</td>
</tr>
<tr>
<td>Brazil</td>
<td>Anvisa</td>
<td>Yes in theory, no in practice</td>
<td>Yes</td>
<td>Both</td>
<td>Concar</td>
<td>Both Anvisa and Concar</td>
</tr>
<tr>
<td>Canada</td>
<td>Health Canada</td>
<td>Legally no/in practice</td>
<td>No</td>
<td>RA</td>
<td>ASC and PAAB</td>
<td>Non-profitmaking organisations, ASC and PAAB</td>
</tr>
<tr>
<td>The Czech Republic</td>
<td>SUKL</td>
<td>No</td>
<td>Some</td>
<td>Both</td>
<td>MAFS</td>
<td>SUKL/MAFS</td>
</tr>
<tr>
<td>France</td>
<td>AFSSAPS</td>
<td>No, but must be submitted to AFSSAPS within 8 days of publication.</td>
<td>Some</td>
<td>Both</td>
<td>LEEM</td>
<td>AFSSAPS</td>
</tr>
<tr>
<td>Germany</td>
<td>HWG</td>
<td>No</td>
<td>No</td>
<td>Both: there are several self-regulatory organisations</td>
<td>FSA</td>
<td>Directly to court system, or by notification of one of the “self-regulatory” regulatory organisations</td>
</tr>
<tr>
<td>Greece</td>
<td>EOF</td>
<td>No</td>
<td>Yes</td>
<td>RA</td>
<td>SFE</td>
<td>Industry association/RA or courts</td>
</tr>
<tr>
<td>Ireland</td>
<td>IMB</td>
<td>No</td>
<td>No</td>
<td>Mostly self-regulation</td>
<td>IPHA</td>
<td>IPHA industry association</td>
</tr>
<tr>
<td>Italy</td>
<td>AIFA</td>
<td>Yes, must be submitted to AIFA 10 days before use</td>
<td>No</td>
<td>Self-regulation</td>
<td>Formindustria</td>
<td>Depends; usual practice is Formindustria, but RA also possible</td>
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(continued)
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<tbody>
<tr>
<td>Japan</td>
<td>MHWW</td>
<td>No</td>
<td>Some</td>
<td>Both</td>
<td>JPMA</td>
<td>IPMA</td>
</tr>
<tr>
<td>Mexico</td>
<td>COFEPRIS</td>
<td>Yes</td>
<td></td>
<td>Both</td>
<td>Code of Ethics of NCR</td>
<td>COFEPRIS</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>MHAWS</td>
<td>No</td>
<td>No</td>
<td>Self-regulation</td>
<td>Naforma</td>
<td>Special commission Medicines Advertising</td>
</tr>
<tr>
<td>Norway</td>
<td>NMA</td>
<td>No</td>
<td>No</td>
<td>Self-regulation</td>
<td>LMI</td>
<td>Norwegian Association of Pharmaceutical Manufacturers</td>
</tr>
<tr>
<td>Spain</td>
<td>No (yes for over the counter, however)</td>
<td>Yes</td>
<td></td>
<td>Controller by regional autonomous authorities</td>
<td>Fama Industria</td>
<td>RA, but also on industry board</td>
</tr>
<tr>
<td>Sweden</td>
<td>SMFA</td>
<td>No</td>
<td>Yes</td>
<td>Mainly self-regulatory</td>
<td>LF</td>
<td>UF, SMFA</td>
</tr>
<tr>
<td>Switzerland</td>
<td>Swissmedic</td>
<td>Yes</td>
<td>No</td>
<td>Both</td>
<td>SSCI</td>
<td>Health Authority and Industry Association</td>
</tr>
<tr>
<td>Turkey</td>
<td>Ministry of Health (MoH)</td>
<td>Yes</td>
<td>Unknown</td>
<td>RA</td>
<td>None</td>
<td>MoH</td>
</tr>
<tr>
<td>The UK</td>
<td>MHRA</td>
<td>No</td>
<td>Limited</td>
<td>Mainly self-regulation?</td>
<td>PMCPA [part of ABPI]</td>
<td>PMCPA/MHRA</td>
</tr>
<tr>
<td>The USA</td>
<td>FDA</td>
<td>Yes</td>
<td>Yes (by DDMAC)</td>
<td>FDA</td>
<td>PhRMA</td>
<td>Appeal to FDA or court</td>
</tr>
</tbody>
</table>

ABPI, Association of the British Pharmaceutical Industry; AFSSAPS, French Drug Agency; AIFA, Italian Medicines Agency; Anvisa, Brazilian Sanitation Agency; ASAI, Advertising Standards Authority for Ireland; ASC, Advertising Standards Canada; COFEPRIS, Federal Commission for Protection against Sanitary Risks (Mexico); CONAR, Brazilian Advertising Self Regulation Council; DEMAAC, Division of Drug Marketing, Advertising and Communication Agency (the USA); EOG, National Organisation for Medicines (Greece); FPHC, French Public Health Code; FDA, Food and Drug Administration Agency (the USA); FSA, Gamer Code of Conduct; HA, health authority; HC, Health Canada; IAMA, Industry Association Medicines Australia; IBS, Irish Medicines Board; IPHA, Irish Pharmaceuticals Health Authority; IPMA, Japan Pharmaceutical Manufacturers Association; IUF, Swedish Association of the Pharmaceutical Industry; IM, Norwegian Association of Pharmaceutical Manufacturers; MAFS, International Association of Pharmaceutical Companies (the Czech Republic); MHWV, Ministry of Health, Labour and Welfare (Japan); MHRA, Medicines and Healthcare Regulatory Agency (the UK); MHWS, Ministry of Health and Sports (the Netherlands); NCP, National Chamber of the Pharmaceutical Industry (Mexico); NMA, Norwegian Medicines Agency; PAGB, Pharmaceutical Advertising Advisory Board (Canada); PMCPA, Prescription Medicines Code of Practice Authority (the UK); SFEE, Hallenic Association of Pharmaceutical Companies; SMFA, Swedish Medical Products Agency; SSCI, Swiss Society of Chemical Industries; SUKI, State Institute for Drug Control (the Czech Republic); TGA, Therapeutic Goods Administration (Australia).