WORKING PAPER SERIES

2005/12

Assessing the Impact of Global Price Interdependencies in a Global Pricing Strategy

Anke Richter

Designing a global pricing strategy for a new pharmaceutical product has become increasingly difficult as geographic reference pricing and parallel trade have introduced global price interdependencies between different nations. What may have been an optimal pricing strategy in a single country may no longer be optimal when considering the international ramifications of this price. The prices set by the pharmaceutical company will affect whether a pharmaceutical prescription product is accepted in each country, whether each country will participate in parallel trade (either as an importer or an exporter), and the prices charged in other countries. It may even affect the desirability of launching a product in a country. After examining lessons learned from a hypothetical case study, the general model formulation is presented. Optimization techniques from the decision sciences can be used to assist pharmaceutical companies with their strategic pricing decisions.

Defense Resources Management Institute
School of International Graduate Studies
Naval Postgraduate School
Building 234
699 Dyer Road
Monterey, CA 93943-5138
831-656-2306
www.nps.navy.mil/drmi

Defense Resources Management Institute
Naval Postgraduate School

The Defense Resources Management Institute (DRMI) is an educational institution sponsored and supervised by the Secretary of Defense and located at the Naval Postgraduate School in Monterey, California. Since 1965 the Institute has conducted professional education programs in analytical decision making and resources management for military officers of all services and for senior civilian officials of the United States and 149 other countries.

The mission of the Defense Resources Management Institute is to educate civilian and military government officials in the principles and concepts of defense resources management.

The unique course offerings create an interdisciplinary, interactive learning environment that facilitates the exchange of ideas among U.S. and international participants in Monterey, California, and locations worldwide. These programs are presented on a regularly scheduled basis at DRMI in Monterey and by specific arrangement at other locations in the United States and in other countries.

The success of DRMI reflects the breadth and depth of the in-house technical expertise that DRMI can draw upon. The DRMI Faculty, a community of scholars and practitioners, are experts in defense resources management and has published in major academic and technical journals. The faculty has extensive experience in providing technical assistance and educational programs worldwide over the past 40 years. Our educational strategy is one of collaboration, tailored to the specific environment of the participant.

The Defense Resources Management Institute specializes in four broad educational areas:

- Economic analysis of the public sector
- Operations research of public sector decision problems
- Public budgeting and fiscal management
- Defense organizations and management methods

For more information about our educational and technical assistance activities, please visit our website at **http://www.nps.navy.mil/drmi** or email us at drmiadmin@nps.edu.

Assessing the Impact of Global Price Interdependencies in a Global Pricing Strategy

By Anke Richter, PhD.[1]

[1] *Defense Resources Management Institute, Naval Postgraduate School, Monterey, CA 93943*

Key Words: geographical reference pricing, parallel trade, global pricing strategy, pharmaceutical products

ABSTRACT

Designing a global pricing strategy for a new pharmaceutical product has become increasingly difficult as geographic reference pricing and parallel trade have introduced global price interdependencies between different nations. What may have been an optimal pricing strategy in a single country may no longer be optimal when considering the international ramifications of this price. The prices set by the pharmaceutical company will affect whether a pharmaceutical prescription product is accepted in each country, whether each country will participate in parallel trade (either as an importer or an exporter), and the prices charged in other countries. It may even affect the desirability of launching a product in a country. After examining lessons learned from a hypothetical case study, the general model formulation is presented. Optimization techniques from the decision sciences can be used to assist pharmaceutical companies with their strategic pricing decisions.

INTRODUCTION

The pharmaceutical industry is faced with numerous issues and competing risks when it sets prices for a new prescription-based product [1,2]. One difficulty when designing a global pricing strategy for a new pharmaceutical product is the existence of global price interdependencies. These interdependencies arise through two primary sources, geographic reference pricing and parallel trade.

Due to pressures on national health care systems, countries frequently choose to regulate and/or set prices for pharmaceutical prices. If the prices are not directly regulated, they are often restricted by reimbursement policies. To help determine the levels at which a drug should be reimbursed, geographical reference pricing (i.e. a comparison of the same product or product class sold in a selection of other countries) is employed. The selection of comparator countries varies for each country practicing geographical reference pricing, but often include countries that have very disparate income levels, gross domestic product, and usage levels of pharmaceutical products. Frequently these benchmarking comparisons are designed to maintain historic price differentials among the countries. While geographic reference pricing originated in Europe, it is now practiced by many countries worldwide [1].

The practice of geographical reference pricing implies that the pricing decision of prescription-based pharmaceutical products in the countries is linked – i.e. the choice of a price in one country may affect the potential prices in a number of other countries.

Parallel trade, the parallel importing of drugs across national boundaries, is another pricing link that pharmaceutical companies need to take into account when designing a global pricing strategy. Parallel trade arises when a third party can purchase the pharmaceutical product in countries with lower prices and resell them to countries with higher prices. Within the free trade zones, such as that seen in the European Union, this activity is no longer illegal and is likely to occur once the price differentials are large enough. Chaudry and Walsh [3] found that a differential of 15% was sufficient for parallel trade to occur in countries that are in proximity to each other. Parallel imports may even be supported by some countries in the hopes of lowering their national health care expenditures. [4,5]

One region, much discussed in the literature, where both parallel trade and global reference pricing occur is the European Union (EU). The countries in the EU are in close proximity to each other and rulings from the European Court of Justice have upheld the free transport of goods, including pharmaceutical products and services, among member nations [6, 7]. Parallel importing among these nations is growing and often nationally encouraged [3, 6, 8, 9]. Member nations have varying market sizes for pharmaceuticals [10]; varying cultural biases in the use of pharmaceutical medications over other forms of treatment [8, 11]; and gross domestic product [12]. There have also been historical price differences among member nations [6, 8-10, 13]. Each country has a national healthcare system and uses nationally established price controls and reimbursement policies to control the cost of these healthcare systems [8, 10, 13-16]. Several member countries engage in geographical reference pricing when determining reimbursement prices for pharmaceutical products in their country [8, 9, 16, 17].

Since the price for a pharmaceutical product set in one market may influence may other markets through these two types of interdependencies, it is important for the pharmaceutical company to examine the impact of a global pricing (and launch) strategy in an analytical fashion. What may have been an optimal pricing strategy in a single country may no longer be optimal when considering the international ramifications of this price. The purpose of this paper is to demonstrate how optimization techniques from the decision sciences can be used to assist pharmaceutical companies with their strategic pricing decisions. The work is conceptual and does not purport to cover all the dimensions of the strategic pricing decision which a company might face in practice. Nevertheless, it demonstrates how optimization techniques can be applied to some of the key elements of the problem.

The paper first presents a small case study of a strategic pricing problem in three hypothetical countries. The case study highlights the issues that surround the strategic pricing decision and the complications that can arise. The global reference pricing policies described are hypothetical but are loosely based on some policies found in Europe. The paper then provides the formulation of the general problem as a mathematical optimization problem and discusses solution techniques. Finally, the discussion presents model limitations and potential model expansions.

CASE STUDY

A pharmaceutical company is considering its strategic pricing decision with respect to a new prescription drug in three countries (Acacia, Beta, and Celsia). The movement of pharmaceutical products among the countries is not restricted and the countries are in close proximity to each other. Each country provides national healthcare to its citizens, including some form of reimbursement of prescription medicines. Since the new product provides therapeutic benefits in a life-threatening illness, the elasticity of demand is very limited. Therefore, in each country, the quantity demanded is constant over time for a range of prices. As long as the price remains within the acceptable range, the country will completely satisfy its demand. However, there exists a price above which the demand goes to zero as countries are no longer willing to provide this medication (believing that the monies could be used to obtain greater improvements in health elsewhere). The maximum price varies by country and is based on the country's historical willingness-to-pay for medications. Let t be the time interval for the model.

All three countries practice geographical reference pricing. Details are provided below with the descriptions of the three countries. A summary of the relevant country characteristics is provided in Table 1.

Acacia : A wealthy country that has a large sub-population ($n = 900$) who would benefit from the new prescription medicine. It has a cultural bias that has led it to be a historically large consumer of prescription medicines and is willing to pay a premium for novel drugs. However, it does not feel that it should carry the other countries' drug burden and once the medication is marketed in another country, it will only permit the average price of the medication, adjusted for purchasing power parity, to be charged. The purchasing power parity conversion rate (the exchange rate between two countries that is the ratio of the two countries' price level of a fixed basket of goods and services) between Acacia and Beta is 1.1 and between Acacia and Celsia is 1.5. Therefore, the price in Acacia is constrained by

P_{Amax} = \$5 / dose

$P_{At} \leq \text{average } \{1.1 * P_{Bt}, 1.5 * P_{Ct}\}$.

Beta : A moderately wealthy country that has a small sub-population (n = 250) who would benefit from the new prescription medicine. It historically has been a large consumer of prescription medicine, but it is wealthy enough that it will pay a moderate amount for novel drugs . Beta firmly believes that it should always pay less than Acacia for its medications since they are not as wealthy a nation. Therefore, it ensures that its price is always 10% less expensive than that which is paid in Acacia unless the product is marketed in all three countries. At this point, Beta feels that the drug is no longer novel and should be priced at a 50% discount of its maximum price. Therefore, the price in Beta is constrained by

P_{Bmax} = \$4 / dose

$P_{Bt} \leq \text{minimum}\{0.90 * P_A, 2\}$.

Celsia : This is the poorest of the three countries, but has a fairly large sub-population (n = 700) who would benefit from the new prescription medicine. Due to the country's financial difficulties, it will only pay a limited amount for novel drugs and insists that its price be less than or equal to the lowest prices charged. Therefore, the price in Celsia is constrained by

P_{Cmax} = \$3 / dose

$P_{Ct} \leq \text{minimum } \{P_A, P_B\}$.

All countries encourage parallel trade and it is 100% efficient (i.e. if parallel trade occurs, the entire market will be supplied with the imported goods). Assuming that an 85% price differential among countries is sufficient to permit the occurrence of parallel trade, then, given the maximum prices that each country will permit, Acacia could import from both Beta and Celsia while Beta could import from Celsia. Celsia can only serve as a source for parallel trade goods.

The pharmaceutical company wishes to maximize the revenue it receives from the sale of its product in these three countries. Mathematically it is maximizing

$$R = \sum_t (D_A * P_{At} + D_B * P_{Bt} + D_C * P_{Ct})$$

Since this case study presents the point of view of the pharmaceutical company, the details of parallel trade including transportation costs and actual price of the good when it is resold are not of interest. For the pharmaceutical company, parallel trade simply represents a loss of revenue (the demand in a given country is supplied with the pharmaceutical product purchased at a lower price in a different country).

The pharmaceutical company can choose to launch the product simultaneously or sequentially in any of the three countries. However, given the geographical reference pricing of the countries, it is not possible to launch the product only in Acacia and Beta. However, it is possible to launch in Acacia and/or Celsia as well as in Beta and/or Celsia without launching in the third country.

The pharmaceutical company may now consider its strategic launch decisions. Let the company employ a 5% discount rate. The 3-year discounted earnings for the 5 best launch sequences are shown in Table 2.

If the pharmaceutical firm wanted to maintain the highest possible price for its medication, it would only launch the product in Acacia. This would allow it to charge $5/dose for all three years. This strategy would produce revenues of $12,867.

If the pharmaceutical firm wanted to capture the large market in Celsia, it could choose to launch either sequentially or simultaneously with Acacia. Launching sequentially would permit the firm to charge the maximum price ($5/dose in Acacia) until it launches in Celsia. Once it launches in Celsia, the price in Celsia would be $3/dose and the price in Acacia would drop to $4.5/dose due to the international benchmarking. However, due to parallel trade, the effective revenue seen by the firm would be for a price of $3/dose (i.e. the price in Celsia, which would become the source of parallel trade for Acacia). Launching in Acacia in year 1 and launching in Celsia in year 2 would produce revenues of $13,425. Launching simultaneously in both countries would allow the firm to capture the larger market one year sooner, but the effective price for the entire market would be $3/dose due to parallel trade. This strategy would produce revenues of $13,725.

Given the choice between Acacia and Beta, it is clear that more revenue can be realized in all launch scenarios involving Acacia since it has both the greater market as well as the higher price. Launching in Beta and Celsia simultaneously provides the greatest revenue involving only these two countries, with a 3-year total discounted revenue of $8,864 – well below the other alternatives presented in Table 2.

The firm could also consider launching in all three countries simultaneously. Given the geographical reference pricing, the price in Beta and Celsia would be $2/dose and the price in Acacia would be $2.6/dose. As the price differential between these countries is greater than 85%, parallel trade would occur for the market in Acacia and the effective price seen by the pharmaceutical firm would be $2/dose. This strategy would produce revenues of $10,580.

Assuming that the strategy chosen with these three countries does not affect the prices in other countries, the pharmaceutical firm would choose to launch in Acacia and Celsia simultaneously as this generates the greatest expected revenue for the firm. Note that the firm would not choose to launch in Beta.

GENERAL MATHEMATICAL FORMULATION

While for small problems it is feasible to examine all possible combinations of launch sequence and price to determine the optimal solution, this approach quickly becomes unmanageable. Considering only two countries (and only two time periods), there are 9 possible launch sequences, for example: A and B simultaneously, A then B, B then A, only A, only B, etc. If three countries were considered (and therefore 3 time periods), there would be well over 50 possible launch sequences. However, the general pricing model for multiple countries can be expressed (and solved) as a mathematical model.

The solution method for this mathematical model will depend in part on the assumptions surrounding the demand function for the prescription pharmaceutical product. If we assume the demand for a prescription pharmaceutical is relatively independent of price, then the problem is a mixed integer linear program and can be solved relatively easily with standard algorithms. If we assume instead that the demand is a function of price, $Q = f(P)$, then the problem is a mixed integer non-linear program because the objective function contains the term $P*Q = P*f(P)$, which is by definition non-linear in P. This problem may still be solved, but it is much more difficult.

Price elasticities in relation to prescription medicines have been found to be very small in absolute value indicating that demand is not very sensitive to price [2, 18]. Therefore, the mathematical model with a demand independent of price is presented. This simplification makes use of the fact that demand for a pharmaceutical product is mostly inelastic up to a boundary price, at which point the product will no longer be purchased at all.

Model Basis and Assumptions

The problem is presented from the point of view of the pharmaceutical company, which is trying to maximize its revenue and hence its return on investment. Geographical reference pricing introduces limits on the prices that can be charged in a given country and are included as a series of pricing constraints. This model assumes that the amount of product that is purchased by individuals in a private capacity (uninsured and/or unreimbursed) is negligible. Therefore, parallel trade is a loss of revenue, and does not provide a means of capturing additional market share.

Constant and variable definitions are provided in Figure 1. The mathematical formulation is presented in Figure 2. The following sections detail the construction of the model.

Objective function

The goal of the pharmaceutical company is to maximize the total discounted revenue over all countries and over all time periods. However, parallel trade causes a loss of income in the country into which the goods are brought since the demand in that country is satisfied by a lower priced product from another country. Therefore, the impact of parallel trade is a loss of revenue and must be incorporated in the objective function as a penalty. Mathematically, this is equation (1).

$$\text{Maximize} \sum_i \left(\sum_t \frac{1}{(1+r)^t} * \left(P_{it} * Q_{it} - LM_{it} * Q_{it} * y_{it} * [P_{it} - Z_t] \right) \right) \quad (1)$$

The second term in the summation of (1) represents the impact of parallel trade and is discussed in greater detail in the following section.

Parallel Trade

If there is a country j whose price is 85% or less than the price in country i, then parallel trade may occur from country j to country i, up to the percent of market share that may be susceptible to loss due to parallel trade in country i, LM_{it}. In the case study in the preceding section, LM_{it} was set to 100% for ease of computation. This is not likely to be the case in a practical application. Chaudhry and Walsh [3] found that only 2 to 10% of the prescription pharmaceutical market was serviced by parallel trade. However, this number is sure to have increased in the intervening years.

If a suitably large price differential exists, y_{it} is equal to 1 indicating the presence of parallel trade. If the price differential between countries i and j is less than 15%, then y_{it} is equal to 0 indicating that there is no parallel trade between the two countries. Since it possible that there may be several countries which have the requisite 85% cost differential with country i, we assume that the parallel importer will choose to import the lowest cost product. When calculating this lowest cost Z_t, it is necessary to ensure that it is the minimum price of all the countries in which the product has been launched. Mathematically,

$$Z_t \leq P_{jt} + (1 - S_{jt})*M \qquad \forall\ i \neq j, t$$

Thus, to determine whether the conditions enabling parallel trade are met, the following equations must hold true.

$$Z_t - 0.85*P_{it} \leq M*(1 - y_{it}) \qquad \forall\ i, t$$
$$0.85*P_{it} - Z_t \leq M*y_{it} \qquad \forall\ i, t$$
$$y_{it} \in \{0, 1\} \qquad \forall\ i, t$$

Therefore, the parallel importer will purchase the product to meet the demand in country i at time t for parallel imports ($LM_{it}*Q_{it}$) from the country which has the overall lowest price (Z_t).

Geographical Reference Pricing

There are a wide variety of geographical reference pricing methods that have been employed by countries. However, as the regulation of pharmaceutical products is a fast developing field, geographical reference pricing practice is also rapidly evolving. All forms of geographical reference pricing can be included as a constraint in the mathematical model. Three types of geographical reference are presented as examples of the types of links that may be present.

Benchmark #1: The price of a product in country i must be 5% lower than the price of the product in a set of reference countries. If the product is not sold in the reference country (S_{it} equals zero), then the constraint is not binding (M is large).

$$P_{it} \leq 0.95 * P_{jt} + (1 - S_{jt}) * M \quad \forall\ t, j \in \{\text{reference countries for country i}\}$$

Benchmark #2: The ratio of the price of the product and its closest competitor(s) in country k must be less than or equal to the ratio of the price of the product and its closest competition in the reference countries in which the product is sold. Let

$$PAlt_{kt} = \text{price of established alternative therapy in country k}$$

If the product is not sold in the reference country (S_{it} equals zero), then the constraint is not binding (M is large). Mathematically,

$$P_{kt} \leq \left(\frac{P_{it}}{PAlt_{it}} \right) * PAlt_{kt} + (1 - S_{it}) * M \quad \forall t, i \in \{\text{reference countries for country k}\}$$

Benchmark #3: The price of a product in country j must be less than or equal to the average price of the product in a set of reference countries. Mathematically, the most obvious representation of this constraint,

$$P_{jt} \leq \frac{\sum_k P_{kt} * S_{kt}}{\sum_k S_{kt}} \text{ if } \sum_k S_{kt} \neq 0 \text{ for } k \in \{\text{reference countries for country j}\} \quad \forall\ t$$

is not linear in the decision variables, (P_{it}, S_{it}), and must therefore be rewritten before it can be included in a linear formulation. This methodology is presented in the Technical Appendix.

Other Constraints

Several other price constraints need to be included in the model. First, prices may only decrease over time.

$$P_{it} \leq P_{it+1} \qquad \forall i, t$$

Secondly, prices must be positive

$$P_{it} \geq 0 \qquad \forall i, t$$

Thirdly, given our assumption with respect to the demand curve, prices must be less than $Pmax_i$, the boundary price, below which there is a fixed positive demand of Q_i and above which the demand drops to zero.

$$P_{it} \leq Pmax_{it} \qquad \forall i, t$$

In addition to these price constraints, there is also a constraint that needs to be placed on S_{it}, the indicator whether or not the product is launched in country i at time t. Once a product is launched it is difficult to pull the product from the market. Therefore,

$$S_{it+1} \geq S_{it} \qquad \forall i, t$$
$$S_{it} \in \{0, 1\} \qquad \forall i, t$$

Taken together, these equations are a mixed integer linear program. A summary of definitions is provided in Figure 1. The complete mathematical formulation is given in Figure 2. Solution algorithms and commercial codes for solving mixed integer linear programs have been available for many years (e.g. see Nemhauser and Wolsey [19]) and are available in numerous commercially available software packages.

DISCUSSION

The model provides a structured analysis of the global strategic pricing problem faced by pharmaceutical companies at the macro-level. It explicitly takes into account the interdependencies that arise during pricing decisions due to geographical reference pricing and parallel trade. Incorporating some simplifying assumptions about the demand curve, the problem is solvable by standard, commercially available software.

The case study shows numerous interesting general results (Table 2). The highest drug price is not always the best option nor is a low drug price always the worst option in a given country. What may have been an optimal pricing strategy in a single country is no longer optimal when considering the international ramifications of this price. This result can already be observed in some pharmaceutical firms' current pricing choices. For example, a new pricing control strategy in New Zealand should have resulted in the prices of ACE inhibitors to be reduced. However, despite new reimbursement limits, the existence of a competitor who product was priced at the low limit, and a documented subsequent loss of market share, some pharmaceutical firms did not lower the price of their ACE inhibitors. The authors of the study suspect that geographical reference pricing is the cause of some of the continued higher prices [20]. Models such as the one proposed in this paper can help in the strategic analysis of these decisions.

This strategic pricing model simultaneously provides the prices and launch sequence for the pharmaceutical product. The variable S_{it} equals 1 when the product is launched in country i. As seen in the case study presented in this paper, some countries may experience long delays due to geographical reference pricing and parallel import concerns. The launch of a product may be delayed until there is a change in the parameters surrounding the questions, such as the introduction of a new competitor who would factor into the reference pricing calculations. For this reason, the general model is a dynamic model capturing expected changes over time. Changes will occur at the latest when a product is no longer patent protected and generic versions can be produced. Delayed launches have already been observed with current pharmaceutical products. In New Zealand, a statin was not marketed due to the low reference price required and subsequent the fears of the impact of geographical reference pricing [20]. In addition, some European countries experience long delays in patient access to pharmaceutical products due to their product pricing and reimbursement policies [11, 14, 17].

The model requires information and data that must be obtained before it can be implemented. The format of international benchmarking policies used by each country in the analysis needs to be ascertained. Some benchmarks are more qualitative than quantitative [17]. These qualitative measures need to be quantified with regards to their typical implementation and influence on the pricing process in that country. Secondly, the market size and likely market share of the product needs to be estimated in each country i and time t to develop the variable Q_{it}. Similarly, the price range over which this demand is likely to hold has to be determined, providing an estimate of P_{max}. Finally, the market share in each country i and time t, LM_{it}, that is vulnerable to parallel imports must be determined.

The model development process employed several simplifications and these can all be considered limitations to the model. A large assumption was the simplified demand function. If we assume instead that the demand is a function of price, then the problem is a mixed integer non-linear program and several new methods and codes have recently become available for this type of problem [21]. A Website (http://www.gamsworld.org/minlp/) has been devoted to practitioners solving this type of problem, providing links to available software and comparisons of different solution methods. However, a more practical solution would be to approximate the objective function by a piece-wise linear function. In particular, it may be feasible to determine price ranges over which a given quantity of demand is inelastic. The successive series of ranges (with fixed demand within the range) would be a piece-wise linear approximation of the demand function and may well summarize the level of detail known about the market place.

The model currently focuses on revenue and does not incorporate the price of launching a product in a given country, the potential interdependencies of launches in different countries, nor the costs of supplying the product to each market. This choice was made to keep the model more tractable.

In the current formulation, the model views parallel trade as a negative, a loss of potential revenue. However, this need not always be the case. Given the issues of parallel trade and international benchmarking, the model predicts that there may be some countries which may experience long delays until the product is officially launched in their country. Some of the demand in these countries may be serviced through parallel imports. In this case, parallel trade would actually be a boon both to the consumer, who has access to the medicine if they can afford the cost of the medicine privately, and to the pharmaceutical firm, who will realize greater sales of their drug. This facet of sales in a country in which the product has not officially been launched can be readily incorporated into the model objective function. In order to do this, it is necessary to estimate the size of the demand for the privately purchased market that may be service by parallel imports. This quantity would then be multiplied by Z_t, the lowest price in the countries which have been launched at time t – assumed to be the source of parallel imports, and added to the objective function. This has not been included in the current model formulation because determining the quantities of demand that will be privately financed is difficult and will depend greatly on the actual price of the medication. This runs counter to the simplified demand function currently proposed. However, this is a feasible model extension, especially if a non-constant demand function is chosen in the general model.

The model does not consider the transportation costs faced by the parallel importer. If there were substantial differences depending on the country of origin, the parallel importer may not always choose the lowest price country as the source for parallel imports (and may indeed choose multiple sources if transportation costs vary by both origin and destination). These costs represent a large amount of data for which the pharmaceutical firm has no readily available source. The model as presented is a worst case scenario in terms of the impact of parallel trade on pharmaceutical revenues.

While the model does not cover all possible complexities encountered by a pharmaceutical firm during its global strategic pricing process, it does provide insight into the issues surrounding geographical reference pricing and parallel trade. As the barriers to importation across nations of pharmaceutical products are lowered and as more countries consider geographical reference pricing as a means of controlling pharmaceutical costs, the global pricing decision becomes more complicated. An analytical means to asses the interdependencies of pricing decisions will become an imperative. The general model formulation provided in this paper is designed to serve as an aid in analytical decision making.

ACKNOWLEDGEMENTS

The author would like to thank Martin Backhouse for his inspiration and invaluable comments during the development of this manuscript.

REFERENCES

1. Gregson N, Sparrowhawk K, Mauskopf J, Paul J. Pricing medicines: Theory and practice, challenges and opportunities. Nature. 2005; 4:121-130.

2. Kolassa EM. Elements of Pharmaceutical Pricing. New York: The Pharmaceutical Products Press, 1997.

3. Chaudhry PE, Walsh MG. Gray marketing of pharmaceuticals. J Health Care Mark. 1995;15(3):18-22.

4. West P, Mahon J. Benefits to payers and patients from parallel trade. (York Health Economics Consortium, University of York, 2003).

5. Kanavos P, Costa-i-Font J, Merkur S, Gemmill M. The economic impact of pharmaceutical parallel trade in European Union member states: A stakeholder analysis. LSE Health and Social Care Research Paper (London School of Economics and Political Science, 2004).

6. Darba J, Rovira J. Parallel Imports of Pharmaceuticals in the European Union. Pharmacoeconomics 1998; 14 Suppl. 1: 129-136.

7. Kanavos P. The single market for pharmaceuticals in the European union in light of the European court of justice rulings. Pharamcoeconomics 2000; 18(6): 523-532.

8. Mrazek MF. Comparative approaches to pharmaceutical price regulation in the European Union. Croatian Medical Journal 2002; 43(3): 453-461.

9. Ess SM, Schneeweiss S, Szucs TD. European Healthcare Policies for controlling drug expenditure. Pharmacoeconomics 2003; 21(2): 89-103.

10. Vogel RJ. Pharmaceutical pricing, price controls, and their effects on pharmaceutical sales and research and development expenditures in the European Union. Clinical Therapeutics 2004; 26(8): 1327-1340.

11. Glynn D. Reimbursement for New Health Technologies: Breakthrough pharmaceuticals as a 20th Century challenge. Pharmacoeconomics 2000; 18 Suppl. 1: S59-S67.

12. http://www.oecd.org/home/ (accessed April 2005)

13. Rocchi F, Addis A, Martini N. Current national initiatives about drug policies and cost control in Europe: the Italy example. Journal of Ambulatory Care Management 2004; 27(2): 127-131.

14. Danzon PM. The Economics of Parallel Trade. Pharmacoeconomics 1998; 13(3): 293-304.

15. Puig-Junoy J. Incentives and pharmaceutical reimbursement reforms in Spain. Health Policy 2004; 67(2): 149-165.

16. Dickson M, Redwood H. Pharmaceutical Reference Prices: How do They Work in Practice. Pharmacoeconomics 1998; 14(5): 471-479.

17. LePen C. The drug budget silo mentality: the French case. Value in Health 2003; 6 Suppl 1: S10-S19.

18. Emilien G. Future European health care: cost containment, health care reform and scientific progress in drug research. Int J Health Plann Manage. 1997;12(2):81-101.

19. Nemhauser GL, Wolsey LA. Integer and Combinatorial Optimization. New York: Wiley-Interscience, 1988.

20. Woodfield A. Augmenting reference pricing of pharmaceuticals in New Zealand with strategic cross-product agreements. Pharmacoeconomics 2001; 19(4): 365-377.

21. Grossmann IE, Kravanja Z. Mixed-integer Nonlinear Programming: A Survey of Algorithms and Applications. In: Biegler LT, Coleman TF, Conn AR, et al., eds., Large-Scale Optimization with Applications. Part II: Optimal Design and Control. Vol 93. The IMA Volumes in Mathematics and its Applications. Berlin, New York: Springer Verlag, 1997.

TECHNICAL APPENDIX

It is possible to linearly express the constraint that a given price be lower than the average price of a select set of international benchmark countries. For example, suppose country D wants to ensure that its price, P_D, is less than the average price of countries A, B, and C. The intuitive formulation for this constraint is

$$P_{Dt} \leq \frac{\sum_k P_{kt} * S_{kt}}{\sum_k S_{kt}} \text{ if } \sum_k S_{kt} \neq 0 \text{ for } k \in \{A,B,C\} \quad \forall t \qquad (1a)$$

However, this formulation is not linear. In order to come up with a linear function to provide us the same constraint, it is necessary to replace (1a) with a series of 7 equations. The following constraints provide the necessary price limitation expressed by (1a):

$P_{Dt} \leq P_{At} + M*(1-S_{At}) + M*S_{Bt} + M*S_{Ct}$
$P_{Dt} \leq P_{Bt} + M*(1-S_{Bt}) + M*S_{At} + M*S_{Ct}$
$P_{Dt} \leq P_{Ct} + M*(1-S_{Ct}) + M*S_{At} + M*S_{Bt}$
$P_{Dt} \leq (P_{At}+P_{Bt})/2 + M*(1-S_{At}) + M*(1- S_{Bt}) + M*S_{Ct}$
$P_{Dt} \leq (P_{At}+P_{Ct})/2 + M*(1-S_{At}) + M*(1- S_{Ct}) + M*S_{Bt}$
$P_{Dt} \leq (P_{Bt}+P_{Ct})/2 + M*(1-S_{Bt}) + M*(1- S_{Ct}) + M*S_{At}$
$P_{Dt} \leq (P_{At}+P_{Bt} +P_{Ct})/3 + M*(1-S_{At}) + M*(1- S_{Bt}) + M*(1-S_{Ct})$

The number of new equations that need to be added to have a set of linear constraints instead of a set of non-linear constraints grows combinatorially with respect to the number of countries used as an international benchmark. In specific, if country D used 4 countries as international benchmarks, it would be necessary to add 15 equations. In general, if country D used n countries, it would be necessary to add
$\binom{n}{1} + \binom{n}{2} + \binom{n}{3} + \cdots + \binom{n}{n}$ constraints.

FIGURE LEGENDS AND FIGURES

Figure 1. Constant and Variable Definitions

Figure 2. Mathematical Model Formulation

Figure 1. Constant and Variable Definitions

Indices and Constants

t	=	year (or other unit of time)
i (j,k)	=	country
r	=	discount rate applied to cost and revenues
Q_{it}	=	the amount of (projected) demand in country i during period t
$Pmax_{it}$	=	boundary price, i.e. the maximum price that can be charged for the product in country i (regardless of the regulatory mechanisms of country i) at time t
$PAlt_{it}$	=	price of established alternative therapy in country i at time t
LM_{it}	=	the market share that is lost in country i at time t due to parallel trade
M	=	an arbitrarily large number

Calculated Variables

Z_t	=	the price in the lowest priced country which will serve as the source for parallel imports at time t
y_{it}	=	indicator of parallel trade in country i in time period t. (binary)

Decision Variables

S_{it}	=	indicates whether or not the product is launched in country i at time t (binary)
P_{it}	=	price of product in country i at time t

Figure 2. Mathematical Model Formulation

$$\underset{S_{it} P_{it} y_{ijt}}{Max}$$

$$\sum_{i} \left(\sum_{t} \frac{1}{(1+r)^{t}} * \left(P_{it} * Q_{it} - LM_{it} * Q_{it} * y_{it} * [P_{it} - Z_t] \right) \right)$$

s.t.

$$Z_t - 0.85{*}P_{it} \leq M{*}(1 - y_{it}) \qquad \forall\ i, t$$

$$0.85{*}P_{it} - Z_t \leq M{*}y_{it} \qquad \forall\ i, t$$

$$Z_t \leq P_{jt} + M{*}(1 - S_{jt}) \qquad \forall\ i \neq j, t$$

$$P_{it} \leq 0.95{*}P_{jt} + (1 - S_{jt}){*}M \qquad \forall\ t, j \in \{\text{reference countries for country } i\}$$

$$P_{jt} \leq \left(\frac{P_{it}}{PAlt_{it}} \right) * PAlt_{jt} + (1 - S_{it}){*}M \qquad \forall t, i \in \{\text{reference countries for country } j\}^{*}$$

$$S_{it} \leq S_{it+1} \qquad \forall i,t$$

$$P_{it} \leq P_{it+1} \qquad \forall i,t$$

$$P_{it} \leq Pmax_{it} \qquad \forall i,t$$

$$P_{it} \leq S_{it}{*}M \qquad \forall i,t$$

$$P_{it} \geq 0 \qquad \forall i,t$$

$$y_{it} \in \{0, 1\} \qquad \forall\ i, t$$

$$S_{it} \in \{0, 1\} \qquad \forall i, t$$

* For ease of exposition, Benchmark #3 was not included in this formulation. To include this benchmark, it is necessary to add the equations developed in the Technical Appendix to the constraint set.

TABLES

Table 1. Summary country characteristics

Country	Acacia	Beta	Celsia
Demand	900	250	700
Max Price	$5	$4	$3
Geographical Reference	$P_{At} \leq$ Average $\{1.1*P_{Bt}, 1.5*P_{Ct}\}$	$P_{Bt} \leq$ Minimum $\{0.90*P_{At}$, 2 (if launched in Acacia and Celsia)$\}$	$P_{Ct} \leq$ Minimum $\{P_{At}, P_{Bt}\}$

Table 2. Total discounted earnings by launch sequence

	Launch ONLY in Acacia		Launch in Acacia Year 1 Celsia Year 2		Launch BOTH Acacia and Celsia		Launch BOTH Beta and Celsia		Launch ALL countries	
	Discounted Revenue	Price/ dose*	Discounted Revenue	Price/ dose*	Discounted Revenue	Price/ dose*	Discounted Revenue	Price/ dose*	Discounted Revenue	Price/ dose*
Year 1	$4,500	$5	$4,500	$5	$4,800	$3	$3,100	$3	$3,700	$2
Year 2	$4,286	$5	$4,571	$3	$4,571	$3	$2,952	$3	$3,524	$2
Year 3	$4,082	$5	$4,354	$3	$4,354	$3	$2,811	$3	$3,356	$2
Total	**$12,867**		**$13,425**		**$13,725**		**$8,864**		**$10,580**	

* This is the effective price per dose seen by the pharmaceutical company due to parallel trade and geographical reference pricing