Enhancing the effectiveness of health care for Ontarians through research

ICES Institute for Clinical Evaluative Sciences

Hospital Funding for New Drug Technologies

June 2002

HOSPITAL FUNDING FOR NEW DRUG TECHNOLOGIES

prepared for the Ontario Council of Teaching Hospitals (OCOTH)

by the Institute for Clinical Evaluative Sciences (ICES)

June 2002

MEMBERS OF THE ONTARIO COUNCIL OF TEACHING HOSPITALS, 2001-2002

Baycrest Centre for Geriatric Care, Toronto
Children's Hospital of Eastern Ontario, Ottawa
Hamilton Health Sciences Corporation, Hamilton
Hospital for Sick Children, Toronto
Kingston General Hospital/Hotel Dieu, Kingston
London Health Sciences Centre, London
Mt. Sinai Hospital, Toronto
Royal Ottawa Hospital Group, Ottawa
St. Joseph's Health Care, Hamilton
St. Joseph's Health Care, London
St. Michael's Hospital, Toronto
Sisters of Charity of Ottawa, Ottawa
Sunnybrook & Women's College Health Sciences Centre, Toronto
The Ottawa Hospital, Ottawa
Toronto Rehabilitation Institute, Toronto
University Health Network, Toronto

ICES Contributors:

Muhammad Mamdani
Michael Paterson
Andreas Laupacis
Kiren Handa
Robert Jacka

Many thanks to Mary Jane Dykeman for her informative legal opinion; to Wendy Cooke for her invaluable assistance in preparation for the OCOTH Report Feedback meeting.

TABLE OF CONTENTS

ICES REPORT ON HOSPITAL FUNDING FOR NEW DRUG TECHNOLOGIES

TABLE OF CONTENTS

APPENDICES

TABLE OF CONTENTS

ICES REPORT ON HOSPITAL FUNDING FOR NEW DRUG TECHNOLOGIES

EXECUTIVE SUMMARY

Background and Rationale

Large academic hospitals are typically viewed as innovators in health care delivery and are often the first to utilize cutting edge diagnostic and therapeutic modalities. Because of the recent advent of a number of new and expensive drugs, there is a concern that hospitals will not be able to afford them, or can only provide these medications at the expense of other important hospital services.

In May 2001, the Ontario Council of Teaching Hospitals (OCOTH) commissioned the Institute for Clinical Evaluative Sciences (ICES) to study these issues, and identify options for how hospitals in particular, and the health care system in general, might optimise the funding and use of expensive new medicines.

Methods

The study was conducted in four phases. First, an environmental scan of both national and international practices of managing escalating hospital drug costs was conducted using the available literature and personal communications. Second, a self-administered survey regarding hospital overall and drug-specific financial information was distributed to all 16 OCOTH hospitals. Third, a telephone survey of each of the OCOTH hospitals was undertaken to better understand approaches used by OCOTH pharmacy and therapeutics committees (PTC) to approve, purchase and monitor drugs. Fourth, a draft of the report was sent to a variety of stakeholders and discussed at a one-day meeting.

Key Findings

Environmental Scan: International Findings

Our international review revealed the Queensland model in Australia to be arguably the most innovative and distinct in inpatient drug approval and management processes. The Standard Drug List (SDL) serves as the central formulary for approximately 150 Queensland public hospitals, contains about 950 chemical entities that have been subjected to clinical and economic evaluation, and is managed by the broadly representative Queensland Hospitals Drug Advisory Committee (QHDAC), which also suggests guidelines for drug utilization. With the exception of drugs covered under a separate Commonwealth-funded "High Cost/Highly Specialized Drugs (HSD)" funding program, medicines prescribed by hospital-based physicians are paid for by the admitting hospital's global budget. While a formal evaluation of clinical and economic endpoints associated with this process has not been conducted, it is Queensland Health's belief that a statewide approach not only avoids duplication and ensures even access, but has the potential to minimize the influence of biases that are more likely to affect formulary decisions made at a hospital level.

Environmental Scan: National Findings

While there is limited information about inpatient drug management across Canada, it appears that in most regions each hospital operates relatively independently with respect to the drug approval process and formulary management. Although this approach offers the highest level of flexibility for individual hospitals, common criticisms of this method include duplication of effort across hospitals and uncertainty as to the quality of the approval process. Discussions towards establishing a central PTC were initiated in New Brunswick but were discontinued due to a lack of a champion to carry the idea forward. On the other hand, the Capital Health Authority of Edmonton and the Winnipeg Regional Health Authority have established central PTC within their respective regions. Discussions are ongoing in Manitoba about a single province-wide formulary process.

Financial Indicators for OCOTH Hospitals

The survey soliciting financial information for fiscal year (FY) 1998-2000 was completed sufficiently by approximately half of the OCOTH hospitals. There was wide variability in aggregate and specific drug-related expenditures, indicating major differences between different OCOTH hospitals. Overall, total hospital expenditures increased more than total drug expenditures over the time period assessed (26% vs. 19%) whereas hospital admissions declined by 2%. Total drug expenditures accounted for approximately 4.3% (range, 2.2-7.6%) of total hospital expenditures. For three-quarters of reporting hospitals, the proportion of total hospital expenditures attributable to drugs decreased during the years assessed. However, nearly one-third of drug expenditures were covered by funding outside the hospital global budget (e.g. through rebates and special programs such as Cancer Care Ontario [CCO] and Special Drugs Program [SDP]).

In contrast, from the government payer perspective of outpatient resource utilization, the Ontario Drug Benefits (ODB) Program has reported an increase in drug expenditures of approximately 50% from 1995 to 2000. Drug therapy is the fastest rising and second largest component of health care expenditures, representing nearly 16% of total health care expenditures by the government in Ontario.

An independent legal opinion regarding the financial responsibility for drugs administered in outpatient clinics indicates that, with some exceptions, neither the hospital nor any specific branches of the Ministry of Health are legally responsible if the sole purpose of the visit is for the administration of medication. This argument illustrates the problem with silo funding, since all Ontario hospitals are ultimately funded by the MOH and therefore hospitals should not be viewed as entities independent of the MOH in this regard.

OCOTH PTC: Structure and Function

All OCOTH hospitals participated in the telephone survey. Only one-quarter of hospitals reported using explicit criteria to grade the strength of the evidence or recommendations for a therapy, and less than one-third of hospitals reported routine input from any individual with advanced training in health economics. Six of the 16 hospitals (38%) reported having formal, written policies for disclosing conflicts of interest. Regular review of relevant decisions taken by other PTC was reported by only one hospital. Perceived levels of confidence in the reviewers' abilities to find, appraise, and understand the relevant evidence varied considerably between respondents. Although numerous interesting strategies

were identified for monitoring utilization following drug approval and containing costs, such as group purchasing and unit-based pharmacists, many argued that resource limitations prevented their broader and more consistent application.

Recommendations

There is a lack of high quality evidence to guide decision-makers in choosing an optimal management approach to hospital drug policy. The single strategy with the most intuitive appeal and face validity is an independent central PTC process that would represent all OCOTH hospitals. The advantages of this approach include provision of sufficient clinical and economic expertise to evaluate drugs, and an equitable decision-making process across hospitals. Initially, only new and extremely expensive drugs warrant consideration by this process. The process would provide non-binding recommendations to all OCOTH hospitals, and should be rapidly expanded to all Ontario hospitals to maximize efficiencies. If needed, hospitals could use these recommendations to solicit new funding for cost-effective medications.

An initial structure for a central PTC process is proposed using the principles of "accountability for reasonableness" outlined by Daniels and Sabin. A **policy advisory committee (PAC)** would review the evaluations provided by an evidence and economics evaluation committee, develop final recommendations for drug approval and conditions for utilization, and disseminate the findings and recommendations to the MOH, drug manufacturers and the public. This committee would be composed of 10-15 members representing a broad range of interests including OCOTH hospital pharmacy members, OCOTH hospital CEOs, practicing clinicians, clinical pharmacists, general public representatives, MOH representatives, and policy experts. An executive subgroup of the PAC representing key decision-makers would decide which drug therapies with promising clinical utility but potentially large financial burdens should be considered for evaluation. The **evidence and economics evaluation committee (EEC)** would be responsible for critically appraising and summarizing available clinical and health economic evidence, predicting expected utilization, and formulating cost-effective guidelines for use of the drugs (indications, dosages, etc.). This committee would be composed of 4-6 core members and 3-4 ad-hoc members depending on the clinical area being considered. The 4-6 core members would be chosen because of their expertise in evaluation, and would represent a broad range of clinical, methodological, and economic expertise. External evaluations from clinical and economic experts would be solicited to strengthen the evaluation process. The **monitoring and evaluation committee (MEC)** will develop and implement appropriate drug utilization and outcomes assessment indicators in OCOTH hospitals to better assess actual drug uptake, financial impacts, and clinical outcomes. This committee would be composed of 7-10 members with broad representation and some expertise in evaluative research.

Benefits to such a process may include improved efficiency and quality of reviews, equity of access to effective therapies, a decrease in the use of therapies that are cost-ineffective, and a potential role for the committee in price negotiations and risk-sharing strategies. Challenges include fair representation of relevant constituencies/committee make-up, timeliness of the decision-making process, need to maintain some decision-making capacity at the individual hospital level, and sufficient funding of the evaluation process.

Summary of Key Findings and Recommendations

- Internationally, the most innovative model for managing inpatient drug utilization appears to be the Queensland (Australia) model of a central formulary, which has been in existence since the 1970s.

- Nationally, the Capital Health Authority in Edmonton and the Winnipeg Regional Health Authority (WRHA) established a central hospital Pharmaceutical & Therapeutic Committee (PTC) in the past decade, and discussions are ongoing about a possible single province-wide formulary process in Manitoba.

- OCOTH hospitals largely operate independently of one another, vary considerably in the perceived quality of their review processes, and may benefit from a centralization of their efforts.

- Because of the vagueness of the current legislation, it is strongly recommended that discussions begin immediately within OCOTH hospitals, and between OCOTH hospitals and the Ontario Ministry of Health (MoH) to clearly indicate whether the hospitals or a particular branch of the MOH is responsible for funding medications provided in outpatient clinics of hospitals.

- It is recommended that a central Ontario-wide OCOTH PTC structure be established to evaluate new and expensive drugs given in hospitals. This would provide expertise in evaluating effectiveness and cost-effectiveness, develop evidence-based prescribing guidelines, and provide equitable access to drugs across the province. This process could rapidly be expanded to include all Ontario hospitals.

- A common approach to drug funding bringing together various drug decision-making bodies such as the Drug Quality & Therapeutics Committee (DQTC), Cancer Care Ontario (CCO), and the proposed central PTC should be explored, since the funding for the drugs approved by these committees all ultimately comes from the MoH.

ICES REPORT ON HOSPITAL FUNDING FOR NEW DRUG TECHNOLOGIES

Introduction

Large academic hospitals are typically viewed as innovators in health care delivery. As they strive to provide optimal care to their patients, they are usually the first to utilize cutting edge diagnostic and therapeutic modalities. Recent concern, however, has been given to escalating drug costs in light of new and expensive technologies that are being introduced at ever-increasing rates. Since the second world war, technological progress has been the single largest contributor to health care costs [1] as up to half of the rise in health care costs may be attributed to the use of new technologies and the misuse of existing technologies.[2] While such costs increase, the resources to acquire these technologies are relatively fixed. Given ostensibly increasing financial pressures in the hospital environment, it is feared that new and effective, yet highly costly medications may not be a viable option under current financial constraints or that funds for other hospital services would need to be diverted to cover increasingly expensive medications.

In May 2001, the Ontario Council of Teaching Hospitals (OCOTH) commissioned the Institute for Clinical Evaluative Sciences (ICES) to study these issues and identify some options for how hospitals might optimise the way in which expensive new medicines are funded and used. This report is divided into four sections. The first section provides a primarily literature-based environmental scan of how various regions, first internationally then nationally, manage drug utilization from both outpatient and inpatient perspectives. The second section focuses on financial considerations and reports the results of a self-administered survey to OCOTH hospitals to examine inpatient drug costs, reviews two major funding sources for OCOTH hospitals (i.e. the Special Drugs Program [SDP] and Cancer Care Ontario [CCO]) and provides an independent legal interpretation of the Health Insurance Act as it applies to the funding of medications used in outpatient clinics located in hospitals. The third section focuses on management issues related to drugs and reports the results of a telephone survey to OCOTH hospitals to examine the composition and functioning of PTCs in OCOTH hospitals. The fourth section serves as a brief review of materials presented and formulates recommendations for OCOTH to consider.

SECTION I. Environmental Scan of Current Drug Management Practices

PART 1. INTERNATIONAL

Summary

(Please see Appendix I for detailed information.)

Increases in drug spending routinely exceed overall health care expenditures, even though many countries have used many methods to attempt to control this at the national or state level. These methods include either direct or indirect price regulation, reference pricing, positive and negative lists and guidelines. However as Willison [3] indicates "There has been little formal evaluation of the success of these strategies. The studies that do exist are primarily descriptive." Frequently a connection is made between aggressive government attempts to control pharmaceutical prices and utilization, and decreased Research & Development (R&D) spending. Increasingly, health technology assessment organizations such as the National Institute for Clinical Excellence (NICE) in the UK and the Pharmaceutical Benefits Advisory Committee (PBAC) in Australia are becoming involved in the evaluation of and recommendations for expensive new drug technologies. "This has important implications for the Canadian Coordinating Office for Health Technology Assessment (CCOHTA) and similar groups in Canada."[3]

The vast majority of countries in collaboration with the Organization for Economic Co-operation & Development (OECD) have special rules for drugs in hospitals, public formularies and prescriptions.[4] (see Tables 3-5, Appendix I) The inpatient drugs are not subject to general price fixing mechanisms but are often included in hospital budgets and may be freely bought through negotiations between hospitals or buying groups and manufacturers.

Pharmacy and Therapeutics Committees (PTCs) are a common and important resource in many countries and at all levels whether, national, state, regional or institutional. Although the make-up varies significantly between committees, physicians and pharmacists are at the core of virtually all PTCs. Pharmacologists and pharmacoeconomic experts are typically under-represented. The main activities involve maintaining a cost-effective formulary, monitoring drug use, and developing and maintaining drug policy and procedures. Although pharmacoeconomic information has increasingly become recognized internationally as an essential component of cost-effective rational drug evaluation, the numerous guidelines often require a level of detail and expertise that is unavailable to most PTCs at an institutional level. Formulary monitoring, drug usage evaluations (DUEs) and prescriber feedback tend to be part of many mandates however they are frequently not happening in any meaningful way. Few standards are available for evaluating the effectiveness of the PTCs or for determining their impact on drug utilization and patient outcomes.

Various cost-containment strategies have been tried. These include (in no particular order):

- prioritization of needs with resource allocation based on cost-effectiveness studies;
- extensive use of DUEs;
- focus on expensive agents;

- therapeutic substitution;
- deletion of non-essential drugs from the formulary;

- prescribing restrictions and fixed budgets;
- addressing the gap between primary and secondary drug formularies;
- prescriber feedback;
- decentralized budget control and monitoring by pharmacists;
- group purchasing, volume commitments, blank purchase agreements, bulk purchasing;
- improved stock control and waste reduction;
- expanding the expertise available to PTCs to enable improved pharmacoeconomic analysis;
- PTC recommendations published alongside projected cost savings;
- education of professional staff on cost-effective use of medications, including current drug price information;
- trial introduction of new medicines followed by DUE and cost-effectiveness evaluation;
- horizon scanning with review of significant new medications prior to federal approval;
- incorporation of guidelines for PTC and DUE from national institutions and organizations;
- use of physicians as 'gatekeepers' representing relevant PTC subcommittees;
- increased involvement and availability of clinical pharmacists to encourage good prescribing practices;
- interdisciplinary involvement in developing local clinical guidelines/critical pathways;
- educating and soliciting active administrative support;
- collaboration with other institutions in the PTC and DUE processes to decrease duplication of effort and improve use of limited resources; and,
- centralized (at regional, state, or national level) formulary committees and drug purchasing.

(Note: Table 8 in Appendix I compares cost-containment approaches used by various countries.)

Unfortunately, evaluation of the effectiveness of these methods is generally lacking. They do, however, reflect the myriad ways in which institutions, organizations and governments worldwide have responded in their common challenge to deal with the increasing pressure on drug expenditures. Duplication of activity is frequently seen as inefficient and unnecessary. Consideration of the wider impact of drug costs on health care utilization inside and outside the hospital is also critically important. However, the shortage of resources to appropriately manage the formulary and drug utilization is a virtually universal problem, which must be addressed if any progress is to be made, especially with the number of potential 'block-buster' drugs that are currently in the pipeline.

PART 2. CANADIAN

Overview

Earlier this year the Canadian Institute for Health Information (CIHI) reported that "drugs continue to consume an increasing share of Canada's health care dollar, accounting for the second largest category of health expenditures next to hospital services." [5] Although the annual rate of increase in overall drug spending from 1992 to 1996 was almost 5%, this rate increased to over 9% from 1997 to 2000. In the Health Canada report, 'Drug Costs in Canada', total hospital drug costs which peaked in 1993, decreased by about 1% per year for each of the following 3 years.[6] (see Table 12 and Figure 3, Appendix II) More recent data is not yet available. However, it has been suggested that this apparently encouraging drop in hospital drug spending is deceptive. Underlying problems include:

- availability of newer, expensive but potentially dramatic therapies is being delayed or restricted;
- funds for other hospital services are being diverted to cover increasingly expensive medications;
- differential access to medicines between hospitals or regions;
- disparity between in- and out-patient availability of medicines;
- new 'block buster' (annual sales greater than $500 million) biotech drugs are coming out of the R&D pipeline at ever-increasing rates;
- inadequate resources have been allocated to the task of managing formularies in a cost-effective manner; and,
- considerable duplication of effort in drug evaluation and drug use monitoring is occurring at the institutional, regional, provincial and national levels.

A number of measures have been implemented by governments at the federal and provincial levels to help control drug prices in Canada. In 1958, the Hospital Insurance and Diagnostic Services Act extended a cost-sharing agreement to the provinces to cover essential hospital services and inpatient medications. Ten years later this coverage was expanded to include physician services. Despite a recommendation from the federally initiated Hall commission to include out-patient prescriptions, this did not happen. The Canada Health Act (1984) replaced the previous legislation, and outpatient medications remain non-essential medical services outside the Act's authority.

In the intellectual property arena, The Patent Act was initially introduced in 1923 and amended in 1969 to oblige patent holders to allow Canadian manufacturers to import their drug in return for a 4% royalty. This was termed compulsory licensing. As a result, generic drug manufacturing increased significantly, but R&D on the part of the pharmaceutical industry dropped because of the decreased financial incentives. With the passage of Bill C-22 in 1987, the period of patent protection was increased and the Patented Medicine Prices Review Board was created. R&D doubled from 5% of sales in 1969 to 10% by 1996. 1991 saw the formation of Bill C-91 as a consequence of the North American Free Trade Agreement and patent protection was further extended to 20 years.[7]

These factors, among others, have had a significant impact on how drug prices are determined in Canada and who pays for them. In addition, the different federal and provincial responsibilities have created increasing tension between these two levels of government. As observed by A.H. Anis, "one key failing of the system is that the federal government is almost completely insulated from the impact of its policies

because, although it regulates drug prices, it does not buy any drugs. In contrast, provincial governments have no jurisdiction over market competitiveness or pricing, yet end up paying for most of the drug expenditures incurred."[8]

National

The Therapeutic Products Directorate (TPD) (formerly part of the Therapeutic Products Program [TPP]) is the Canadian equivalent of the FDA in the United States. Its primary responsibility is to ensure the safety and efficacy of new drug entities before they can be introduced into the Canadian market. There are up to eight core members of the TPD's Expert Advisory Committee on Pharmacovigilance each with up to a four year term. Representatives include experts from medicine, pharmacy, basic and applied biomedical sciences, pharmaco-epidemiology, and ethics, as well as those who communicate health policy issues. The main activities of this committee are: to follow-up evaluations of post-approval drug safety, quality, efficacy and effectiveness; and to make recommendations for research and educational programs both for professionals and consumers. (see Table 11, Appendix II)

In FY 1994/5, the TPP Cost Recovery Initiative was introduced as a "federal government policy initiative that requires government departments to consider charging appropriate fees for qualifying services. It is a means of transferring some or all of the cost of a government activity from the general taxpayer to those who more directly benefit from or who 'trigger' special activity."[9] Special activity includes drug evaluation. This may be an avenue to help offset the costs incurred in the thorough and expensive review process at the national, provincial or possibly sub-provincial levels.

The Patented Medicines Prices Review Board (PMPRB), a quasi-judicial body, reviews the prices initially proposed or later charged by the pharmaceutical manufacturers to ensure they are not excessive. Excessiveness is defined based on the context or category into which the drug falls. Category 1 drugs are usually new products that merely offer a new strength or formulation of an existing medicine, and are commonly referred to as 'line extensions'; Category 2 drugs are called 'breakthrough or substantial improvement drugs' because they are either the first drug to treat a particular disease or offer substantial improvement over existing therapies; Category 3 drugs offer minimal if any improvement over existing drugs and are often called 'me-too drugs'.

There are three guidelines that determine if the price of the new product is excessive. The first is that the price of an existing patented drug may not increase more than the Consumers' Price Index (CPI); second, the price of a new drug must remain within the range of prices for drugs of the same therapeutic class; and third, breakthrough drug prices may not exceed the median (or the highest if no median exists) price charged for the drug in seven other countries including France, Germany, Italy, Sweden, Switzerland, Britain and the US. The PMPRB has the authority to enforce these guidelines and require restitution from the manufacturers if prices have been deemed excessive.

In 1987, drug prices were about 23% higher in Canada than in any of the seven other comparison countries except the United States. As of 1999, however, Canadian prices were on average 10% below these median values. Breakthrough drugs, which accounted for about 12% of drugs reviewed in 1997 by the PMPRB, have a particularly significant impact on pharmaceutical expenditures as well as drug prices since they are usually more expensive, and may establish a new therapeutic class, thus setting a reference price for that class.

Since there are several major departments and other responsibilities that fall under federal jurisdiction (such as the Department of Defense, the Veterans Administration and the Non-Insured Health Benefits Branch of Health Canada), the Federal PTC is charged with the review of new drugs as requested by the participating agencies. This committee makes recommendations to the respective departments. The recommendations are based on their review of clinical studies (ideally published in peer-reviewed journals) comparing the new product to current therapies, clinical data (which should demonstrate efficacy and any toxicities), a complete bibliography with search strategies included, current pricing and a pharmacoeconomic evaluation which conforms to the Ontario Ministry of Health (MoHLTC) and the Canadian Coordinating Office for Health Technology Assessment (CCOHTA) guidelines showing benefit related to cost as well as alternative therapies.

The National Drug Scheduling Advisory Committee (NDSAC) was established in 1995 by the National Association of Pharmacy Regulatory Authorities (NAPRA). Advising provincial pharmacy regulatory authorities regarding placement of drugs within the 3 schedule/4 category, national model is its primary function. Members meet up to four times a year and are selected on the basis of having Canadian expertise in pharmacotherapy, drug utilization, drug interactions and toxicity, pharmacy practice, academic research, the drug industry and pharmaceutical regulation at federal and provincial levels. The Consumer's Association of Canada is also represented.

Federal-Provincial Discord

"The lack of data which provides comprehensive drug use and cost information across government jurisdictions, is a major barrier to improving drug utilization in Canada. A project is currently underway to explore a coordinated, common approach to drug utilization data, analyzing drug costs and outcomes: The Options for Prescription Drug Utilization Study (OPUS), funded by the Health Transition Fund and CIHI."[10] A set of core indicators for the project was published by CIHI in March of this year.[11]

In the Health Canada report, 'Drugs Costs in Canada', released in 1997, the uncoordinated approach of the various stakeholders (public and private payers) in response to increasing drug costs "has produced trends which appear to be at odds with Canadian policy directions for health care." As noted by Anis[8], as a consequence of Bills C-22 and C-91, "federal and provincial policies have moved in opposite directions". There is no indication that any significant or consistent cooperation is occurring between the provinces and the federal government with respect to drug evaluation and utilization. Duplication of effort appears to be the rule rather than the exception here.

In 1998, the Prescription Drug Utilization Standards and Reporting System (PDUSRS) project was launched to "develop data standards and a reporting system for prescription drug utilization in Canada." (http://www.cihi.ca/Roadmap/Prescript_Drug/briefing.shtml, updated Mar 2001; accessed) Guiding this group is the National Drug Utilization Advisory Group (NDUAC), which is composed of experts in drug utilization research, policy makers, drug plan administrators, professional associations and consumers. The indicators focus on community based prescription drug use as opposed to hospital or other institutional use.

Another entity formed in 1998 represents federal, provincial and territorial interests, and is known as the F/P/T Pharmaceutical Issues Committee (PIC). Members include government officials from each province and territory as well as from Health Canada and other federal departments and agencies. The

two-year program was designed to examine issues affecting drug prices, drug use and system inefficiencies and to follow up with recommendations.

Provincial

"Over the seven year period (1990-1997), the six provincial drug plans saw a 44% increase in expenditures. During that same period, price changes in the six provincial drug plans ranged from increases of 7% to declines of 11%. Other factors (i.e. changes in utilization of existing medicines, and the introduction of newer, costly drugs) have therefore accounted for the majority of the 44% increase."[12]

The provinces have implemented several mechanisms in their attempt to control drug prices such as formularies, generic substitution, reference-based pricing (also called therapeutic interchange), price freezes, controls on mark-ups and dispensing, and risk sharing.

The Ontario Drug Benefit (ODB) program, established in 1974, was the first provincial effort to provide drug benefits for seniors and those requiring social assistance. The other provinces have implemented similar programs since that time, although the drug coverage varies considerably. Despite the fact that drug manufacturers claim to provide essentially the same information to each of the ten provincial formulary committees, the decisions reached are often very different. This was demonstrated in a recent study by Gregoire et al which examined nearly 150 drug entities introduced between 1991 and 1998, and found, for example, that of the 23 new cardiovascular drugs, one province (Prince Edward Island) had eight and another (Manitoba) had 22.[13] This has prompted criticism from those in the drug industry suggesting that the economic analyses prepared, according to CCOHTA guidelines, are frequently ignored by governments in the decision-making process. An additional criticism is that formulary decisions are often made on the basis of drug price alone rather than considering the overall cost-effectiveness, namely the possible cost savings to health expenditures outside the drug budgets.

In the 'Saskatchewan Task Force on High Cost Drugs'[14] the report noted that the "difficulty of getting any interjurisdictional agreement will be obvious", and the "different stance taken by provincial governments over the coverage of Betaseron and Copaxone is yet another example of different reactions to the same information." In light of the "considerable opportunity to work collaboratively with other provinces", the authors encouraged Saskatchewan to share information, consider a common submission process, and create a list of priority areas requiring pharmacoeconomic study which could be tackled collectively or by contract with another agency such as CCOHTA.

The disparity between provincial formularies has also been described as 'a dog's breakfast' by Anis et al in a recent review of Canadian prescription drug coverage. Of their sample of 58 drugs (which constituted the majority of new drugs seeking formulary inclusion in Canada during 1996 and 1997), the overall measure of agreement among the 10 provinces was only 20%. Category 3 ('me-too') drugs were more likely to be approved and there was "a significant association between therapeutic classification and coverage decision." However, inclusion rates were relatively flat across disease groups.[15]

Given this disjointed approach to drug coverage, a desire to establish a national formulary is increasing. The National Forum on Health report released in 1997 by the Minister of Public Works and Government Services, "viewed pharmaceuticals as medically necessary and considered public funding of a national

drug plan as the only way to achieve the dual goals of universal access and cost control." The following year, the Conference on National Approaches to Pharmacare recommended that a "National program based on the principles of universal access, first-dollar, single-payer pharmacare delivered through provincial programs" be established. This has yet to happen. However, there has been some recent indication of movement in this direction. In the September 25, 2001 edition of the Toronto Star, the provincial and territorial health ministers expressed interest in working with the federal government to develop a national approach to bulk drug purchasing and evaluation. "We're looking for ways to simplify and reduce the amount of duplication that takes place in the review of new drugs" as well as reducing drug costs, said Newfoundland Health Minister Julie Bettney.

Funding for special drug programs has also been created in such areas as cancer, HIV and cystic fibrosis.

Despite these efforts, however, pharmaceutical expenditures have continued to increase significantly - as outlined in Table 15, from 1990 to 1997. "They are now one of the fastest growing components of total health care expenditures in Canada, and in 1993, for the first time, drug costs exceeded payments to physicians."[8]

Provincial PTCs

(see Tables 13, 14, Appendix II)

Most of the provinces have either one or two committees, which have the responsibility for drug evaluation and formulary recommendation and maintenance. British Columbia (BC) is the exception with five, however there are two primary bodies (the Therapeutic Initiative [TI] and the Pharmacoeconomic Initiative [PI]) which govern formulary decisions for that province. Standing subcommittees are common, but in some provinces they are convened on an ad hoc basis. All provinces have physician, pharmacist and government representation, and all but New Brunswick, Newfoundland and Labrador utilize pharmacology expertise. Economists are also frequently involved but that is where the similarities in make-up end. Biostatisticians, chemists, dentists, epidemiologists, lawyers, nurses, pharmacokineticists, veterinarians and other representatives can be found in some but not all of the provincial formulary committees.

The number of individual committee members varies from as few as two in the Prince Edward Island (PEI) Pharmacy Benefits Committee to as many as 20 in BC's TI. Meetings take place for many committees on a monthly or bimonthly basis, but in some cases as infrequently as two or three times a year.

In terms of the proportion of seniors relative to all active provincial drug plan beneficiaries, this varies from a low of under 20% in Saskatchewan to a high of almost 2/3 in Nova Scotia.[15] This factor obviously has a significant impact on formulary decisions both on the money available for drug benefits and on the medication needs and therefore expenditures for each province.

All provinces have committees which consider efficacy and cost in the drug submission process. Most of them require data which compares the new drug to existing therapies, and most also either require or often use the CCOHTA pharmacoeconomic guidelines. The chief differences tend to be found in the type of cost information required and how that information is used.

Based on available information, several of the provincial committees review over 200 drug products annually, with a two-four month interval between successful submission and final decision, in part depending on whether the drug is a single or multiple source item.[16] The New Brunswick Provincial Drug Plan restricts drug review requests to physicians in an attempt to base evaluation on an indicated need rather than on a pharmaceutical manufacturer's desire. This, of course, can be subverted with the assistance of an agreeable physician.[17]

The BCPI indicated in its FY 1999/2000 report that it is capable of performing various types of impact analysis including financial, utilization and substitution either retrospectively or prospectively. However, even though several provincial committees have some sort of monitoring, ongoing evaluation or educational responsibility, information as to how these functions are performed is not readily available.

Although the composition of the expert advisory committees and the drug evaluation process may differ across provincial drug plans, the intended goals of the various processes are similar and involve both therapeutic and cost impact issues. However, the extent to which ongoing monitoring of the effectiveness of PTC activities and DUEs are being conducted is either unclear or extremely limited.

The Ontario MoHLTC Drug Quality And Therapeutics Committee (DQTC)

The DQTC was established by Order in Council #2217/68 in 1968 as an expert advisory group to provide independent and specialized advice to the Minister of Health and the Drug Programs Branch on drug-related issues. The committee evaluates both the therapeutic value and cost effectiveness of brand drugs submitted for reimbursement under the Ontario Drug Benefit (ODB) Program, and makes recommendations on the interchangeability of generic drug products. It also provides recommendations to the Ministry, on a case-by-case basis, about coverage on thousands of requests received each year for drugs not listed in the ODB Formulary through the Individual Clinical Review (Section 8) mechanism. A comprehensive roster of consultants/reviewers also exists to assist the DQTC in the review of drug product documentation and other drug-related issues. The services of these consultants/reviewers are obtained to complement the expertise available on the DQTC.

Currently, the DQTC meets monthly and has 12 members including its Chair. Members include representatives from medicine, pharmacy, pharmacology, epidemiology, health economics and other disciplines, specifically chosen for their technical expertise, training, and/or knowledge.

The Committee's terms of reference are:

- to advise the Minister on the operation of programs designed to assist Ontarians in obtaining prescribed pharmaceutical products of quality at reasonable cost;
- to establish, maintain, and apply criteria to evaluate the quality and therapeutic value and cost of drug products, to recommend to the Minister those products which should be considered for publicly funded drug programs, and to advise the Minister of the conditions under which such products should be funded;
- to recommend to the Minister, which drug products should be designated as interchangeable products or listed drug products for the purposes of the Drug Interchangeability and Dispensing Fee Act, and the Ontario Drug Benefit Act;

- to continually monitor and evaluate the list of drugs available in the light of drug use patterns, experience and current scientific knowledge;
- when requested, to contribute and support ministry efforts on education about publicly funded drugs and related issues;
- to review and assess information related to drugs and pharmaceutical products prepared for the Committee and the Minister by selected consultants, as requested by the Minister;
- at the Minister's request, act as liaison between the Minister and professional, educational and other groups; and
- to provide advice on relevant drug, pharmaceutical, policy and therapeutic questions and issues solicited or requested by the Ministry of Health, from time to time.

Contents and review process for submissions to the DQTC

A complete submission undergoes a thorough review by the DQTC. The DQTC considers several factors during its review, including objective evidence of safety and efficacy in comparison to listed alternatives, and evidence supporting the cost effectiveness of the product. Following its review, the DQTC makes recommendations to the Ministry as to whether a drug product should be listed as a Formulary benefit and whether it should be designated as interchangeable. The following provides a brief overview of the contents of and review procedures for submissions to the DQTC. Further details can be found at the Ministry's website (www.gov.on.ca\health).

Contents of the Submission

To be considered by the DQTC, each submission must contain the following:

- evidence of Health Canada's approval;
- a consent letter allowing communication with Health Canada, other provinces/territories, and the Patented Medicine Prices Review Board;
- a proposed Drug Benefit Price;
- a letter confirming ability to supply anticipated demand for product at Drug Benefit Price;
- clinical evidence;
- pharmacoeconomic evidence; and
- a written agreement.

Clinical evidence is defined as "clinical studies and, if available, other clinical evidence of the product's therapeutic effectiveness or efficacy and of the product's safety, including any information that relates to adverse drug reactions and any existing clinical studies comparing the product's therapeutic effectiveness or efficacy and the product's safety to that of other products or treatments."[18] Manufacturers may satisfy this requirement by submitting a completed Clinical Data Checklist (Table 16, Appendix III) and a comprehensive summary of all critical studies, along with a bibliography of all published and unpublished research. The Clinical Data Checklist is based on the guidelines that DQTC reviewers use during their evaluation of a submission, and is designed to help manufacturers prepare submissions that are easy to review and to ensure submissions proactively address the DQTC's usual questions. For each question on the Clinical Data Checklist, manufacturers are asked to provide a short answer and direct reviewers to the supporting reference pages.

Pharmacoeconomic evidence is defined as "evidence demonstrating the benefit of the product in relation to the cost of the product and to any alternative products or treatments."[18] Manufacturers may satisfy

this requirement by submitting a completed Pharmacoeconomic Analysis Summary; a completed Pharmacoeconomic Worksheet (Tables 17 and 18, Appendix III) and study, if applicable; and a Financial Impact Analysis Summary (Table 19, Appendix III). The Pharmacoeconomic Worksheet and instructions for how to prepare an economic analysis are derived from the Ontario Guidelines for Economic Analysis of Pharmaceutical Products[19].

The Ministry and the DQTC are interested in evaluating the value-for-money of new drug products, particularly in comparison to alternatives already listed in the ODB Formulary. While not all submissions require a full cost-effectiveness analysis, some form of economic evaluation and summary is necessary for all products. A starting point is the tabulation of costs of therapy associated with the submitted product and appropriate comparators, and an itemization of the important respective outcomes (the Pharmacoeconomic Analysis Summary). When drugs are equally effective and have similar side-effect profiles, a comparison of total costs of therapy alone (i.e., a cost minimization analysis) may be appropriate. In situations where the new product actually improves outcomes at a lower cost (i.e., dominant therapy), then a cost minimization analysis is sufficient. If the new product has an incremental cost (drug price and/or total therapy cost) with an incremental gain in efficacy or other outcomes, then a cost-effectiveness, -utility, or -benefit analysis is indicated. Cost-utility analyses are required when the value of the therapy relates to improvements in quality-of-life. As cost impacts outside of drug expenditures are important in the evaluation of pharmaceutical products, these costs should be itemized carefully and realistic unit costs should be assigned from standard reference sources (e.g. case costing systems in hospitals, schedule of benefits for physicians and laboratories).

The Financial Impact Analysis provides both the Ministry and the DQTC the opportunity to understand the impact of a new drug product on Ministry expenditures. The DQTC considers the analysis in conjunction with the pharmacoeconomic data in assessing the incremental and overall cost considerations of a new product. This forecast also is use by the Ministry (when a positive recommendation has been received from the DQTC) to develop ODB expenditure forecasts and to assess written agreements (see below). For manufacturers, basically, the forecast entails an estimate of yearly expenditures (drug costs only) for the product under consideration for three consecutive twelve-month periods. Assumptions underlying the forecast include:

- a summary of potential market size, rate of growth, and extrinsic factors that may affect market size;
- initial market capture and how entry impacts existing Formulary product utilization (including rates of growth/decline of other comparators);
- an estimate of the average claim cost and number of claims underlying forecast; and
- anticipated changes, including generic entry or the entry of new competitor drugs, that may affect market share projections.

The Financial Impact Analysis Summary sheet was developed to assist manufactures with this section of the submission.

The last component of the submission is a written agreement. Written agreements were introduced in June 1998 as a condition of listing for all new single source products recommended for listing in the ODB Formulary. Here, the manufacturer of a product must enter into an agreement with the Ministry which includes the net forecasted costs (as above) to the ODB Program in the three-year period commencing the day the product is listed. While the Ministry encourages manufacturers to submit a draft agreement at the

time of submission, since the conditions for listing, if any, may be difficult to predict at the time of submission, in reality an agreement is not required from the manufacturer until a positive recommendation for listing is made by the DQTC. If the Ministry accepts the forecasted costs, the product is referred to government for consideration for listing in the Formulary. If the Ministry has concerns about the projections, the manufacturer is notified and may meet with Ministry staff to discuss its forecast and the underlying assumptions. For further information about the implications of this agreement, readers are direct to the Ontario Drug Benefit Act.

Although the submission requirements must be met in order to initiate the review process, the Ministry or DQTC may request additional information any time during the process to address uncertainties associated with a submission or to resolve questions which may have arisen. Manufacturers are free to withdraw a submission at any time.

Process for reviewing and approving a Submission

Once a submission is determined to comply with the regulations, its status is noted as complete and the submission is sent to one or more DQTC reviewers. Submissions are reviewed by DQTC members and/or by reviewers drawn from a roster of external consultants. The targeted time frame for the reviews is four weeks. However, submissions that are considered to be particularly complex by reviewers or Ministry staff may require more time, and occasionally a panel or subcommittee of the DQTC may be struck for a specific review.

Submissions are considered by the DQTC in a pre-specified order. "First Review" submissions, both single source and multiple source, are considered first on the DQTC meeting agenda. After first review submissions, second review submissions and finally reconsideration submissions are considered on the agenda. Within each category (first review, second review, reconsideration), submissions are ranked on the agenda according to the date each submission is deemed complete. Products designated for "fast tracking", as determined by the DQTC Chair or Ministry Staff, are given preferred status on the agenda. Such products are:

- new chemical entities that represent new drugs effective for the treatment of immediately life-threatening diseases and other serious diseases where no comparable drug is marketed in Canada;
- new drug products that will have a significant impact in reducing Ontario's Ministry of Health and Long-Term Care expenditures (more than $1,000,000 in savings per year); or
- drug products that offer significant savings (more than 35% and at least $250,000 per year) to the ODB program.

The DQTC has five main options in making a recommendation regarding a product:

- general listing (with no restrictions);
- limited use listing (covering patients who, according to the prescriber, meet pre-specified clinical criteria listed in the Formulary);
- reimbursement through a pre-approval mechanism (whereby individual written requests by prescribers undergo either individual clinical review or expedited review with criteria (Section 8));
- facilitated access (for specific products used to treat ODB eligible persons with HIV or AIDS); or
- no reimbursement under any circumstances.

If a recommendation has been made for Limited Use or Section 8, a subcommittee may be asked to formulate the criteria for coverage.

The committee's final recommendations are drafted into minutes, which are generally ratified by fax within 14 days of the DQTC meeting, and it is these minutes, which form the basis of communication to the manufacturer. Where the DQTC has rejected a product for listing, the issues or concerns raised by the DQTC are summarized for the manufacturer. Where the DQTC has recommended a product for listing, the communication will state the proposed reimbursement status (including details of the reimbursement criteria to be applied through Section 8), and that the product will proceed to the next stage in the evaluation process. A positive recommendation by the DQTC is not a guarantee of listing in the Formulary; however, in practice, such decisions are rarely overturned.[20]

For negative judgements, the manufacture must respond to the DQTC's concerns within six weeks in order to maintain the submission's existing review ranking. Late responses are considered as the DQTC agenda permits. Reviewers are given four weeks to consider a manufacturer's response and file their reports with the Ministry and the review is deemed complete and scheduled as a "Second Review" agenda item at the next available DQTC meeting. At this meeting, the DQTC discusses the submission, with input from the reviewers, other external consultants, and the Ministry, and employs the same decision options used in the First Review. If the manufacture's response is deemed inadequate, a negative recommendation is issued and the submission loses its ranking in the submission review cycle. Manufactures are given six months to prepare a final response; such submissions are reconsidered by the DQTC as their agenda permits. If a manufacturer fails to address the outstanding issues within that time frame, the submission is withdrawn and subsequently destroyed.

Throughout this process, all documentation and correspondence must be directed to the Ministry's Drug Programs Branch, and not to the DQTC, its chair, or any members or consultants to the committee. Direct approaches (in any form) to DQTC members, in their capacity as members of the committee, may be viewed as introducing a conflict of interest and might create an appearance of bias or unfairness on the part of committee members. Such contacts may result in a delay in a decision about a product and may put a submission at risk for withdrawal.

The Ministry continues to make efforts to increase the level of transparency of the submission and review process. In 1996, measures were introduced to increase the frequency and nature of communications with manufacturers and to permit manufacturers with access to technical portions of reviewers' reports. The status of submissions and the rationale supporting DQTC and Ministry decisions are also available to the public. If a manufacturer has concerns about a competitor's submission or listing, the Ministry will accept any information that the manufacturer believes is relevant to the consideration of the competitor's product. This information may be shared with the DQTC and the competitor for their consideration and comment, at the Ministry's discretion.

Cost-containment (Out-Patients)

An assessment of the impact of high cost drugs on the Saskatchewan formulary[14], found that although pharmacoeconomic guidelines were sometimes used, the Saskatchewan Formulary Committee (SFC) was "not constrained by a budgetary ceiling", that it considers the merits of new drugs and their value for money often independent of a larger socio-economic context.

Another paper, released in August 2000, examined Alberta's drug cost containment strategies. [21] As of 1993 the acquisition costs were limited to the lowest cost alternative, and a flat dispensing fee was

introduced. The following year seniors' co-insurance rate was increased to 30% from its previous rate of 20%, and a co-payment ceiling of $25 per prescription came into effect. Two of the major findings were that total provincial savings attributable to these changes from 1993 to 1999 was over $180 million, and the lowest cost alternative and dispensing fee changes substantially decreased total drug costs. Annual drug expenditures however continued to increase "at a remarkable rate". The authors noted the limitations of the restricted focus on drug as opposed to health expenditures and the absence of patient outcome information. Drug costs were driven mainly by increased utilization and by expensive, new products.

Regional (Inpatients)

Winnipeg Regional Health Authority (WRHA)

Established in 1999, the WRHA is one of twelve Regional Health Authorities in Manitoba, and the provincial leader with respect to central formulary management. See Section II for more information.

Simon Fraser Health Region

The SFHR provides health care to over 1/2 million residents, with 4 acute care facilities and over 3,000 long term care beds. Formulary management processes vary considerably in British Columbia between regions and hospitals as well. However, although the high cost of new drugs is definitely a concern, the challenge to provide appropriate access to good medicines while controlling costs has generally been successful. No further information was available to clarify this observation.

Provincial funds directed towards particular patient groups such as those with cancer and HIV/AIDS, tend to cover only directly relevant medications resulting in inadequate funding for what is deemed more peripheral such as symptom management.

Suggestions were made to strengthen the federal drug review process to include relative value in comparison to currently available agents, and to minimize conflicts of interest in the decision-making process.[22]

South-East Health Care Corporation, NB

The concern over the increasing rate of in-hospital drug is a concern in this part of the country as well. There are 8 health care corporations in the province, each with separate PTCs, in addition to the provincial formulary. As a result, there is much duplication of effort between hospitals, government and third-party payers that could be reduced with more collaboration. Two of the larger hospitals also have DUE services and make their evaluations available to the PTCs throughout the province. The formulary processes of the 8 committees are assumed to be quite similar with patient quality of care as the first concern. The need for future ethics support also has been identified.[23]

Managing High Cost Drugs

In the last 5 years, about 55% of the increase in drug costs has been due to cancer treatment, and about 40% has been due to cardiac and coagulation related therapies. In situations involving a high cost-burden

medication with proven benefit, appropriate Program and corporate administration will develop a means to address the issue. However, the most significant problem faced is that of inadequate resources to complete the rigorous cost-effectiveness evaluations required to assess the total impact of the numerous new medicines being introduced to the health care system. This underscores the importance of collaboration at all levels of government to provide this high quality analysis in a timely fashion.

The only additional program which supplements the hospital corporation drug budgets is the Erythropoetin Program in the Dialysis Centres. Due to the significant costs increases associated with oncology therapies, there is a need for a provincial cancer care program. Additionally, the expensive new therapies in areas such as Ophthalmology and Rheumatology given to outpatients in hospital have also been a significant cost burden to the hospital drug budget. Third party payers and the NBPDP have yet to address these issues.

Ottawa Valley Drug Information Services (OVDIS): Formulary/Drug Utilization Project

This regional DUE funded by a 2 year Hospital Incentive grant was designed to examine these issues in a larger scope.[24] As the author notes, "Traditionally, DUE has been conducted in large teaching hospitals, which possess the necessary resources. A prototype does not exist for conducting these evaluations on a regional basis, nor for various hospital sizes. Small institutions do not have the staff, time or expertise to attempt an evaluation of their drug utilization."

This retrospective study of oral ciprofloxacin involved 21 OVDIS hospitals, and required 2 full-time staff, a voluntary advisory group of 2 pharmacists, as well as infectious disease specialists, a biostatistician and a computer consultant. 70% of the hospitals had never completed a DUE before, and this lack of familiarity with the potential benefits of this process, along with the significant resources required, made some hospitals reluctant to cooperate.

Ultimately in the 19 participating hospitals, inappropriate use of and inappropriate justification for cipro was found in 96% and 92% of the cases, respectively. The cost analysis suggested that a cost savings of almost $70,000 (presumably per hospital and presumably with 100% appropriate use of oral cipro, although the article does not specify). The study, although primarily descriptive, was apparently hampered by lack of resources itself; thus the implications and the actual impact of the study on prescribing behaviour, patient outcomes and cost savings could not be followed up.

Institutions

In British Columbia, D'Sa et al[25] compared the rates at which new drug therapies were added to the formularies of 6 teaching and 25 non-teaching hospitals. Using the dates between Canadian market approval and formulary acceptance for 29 drugs, they found a significant difference with teaching hospitals taking only 7.5 months as opposed to 12 months in the non-teaching facilities. In a follow up article[26], D'Sa explored the possible reasons for this difference using Rogers' Diffusion of Innovation Theory[27] The major factors influencing adoption of a new drug (or any innovation) include:

- relative advantage or superiority over existing options;
- compatibility with existing community values;
- complexity of use;
- trialability, or ability to test the drug before incorporating it into the formulary; and,
- observability, or the degree to which the therapeutic effects can be recognized.

Roger's model to predict the speed by which facilities will accept new technology is based on a bell curve distribution:

- innovators (2.5% of users);
- early adopters (13.5%);
- early majority (34%);
- late majority (34%); and,
- laggards (16%).

The study found that several teaching hospitals could be considered to be innovators, the remainder either early adopters or early majority users; while several non-teaching hospitals could fit into the early to late majority group with the remaining hospitals, requiring 2-3 years for approval, possibly placed in the laggard group. This may indicate that teaching hospitals are more motivated, skilled or better equipped, or that non-teaching hospital committees are more skeptical of, or reluctant to introduce, new medications. However, the authors clearly state that several significant factors may complicate the interpretation of their findings. High drug acquisition costs may have prevented formulary inclusion, and the cost of new drugs as a factor was not examined. Some of these new drugs may have still been available using a non-formulary process. And investigational use of drugs before the NOC date was also not surveyed. Despite the study's limitations, the leadership role that teaching hospitals play and the market forces influencing adoption of new technologies are important factors to consider in this discussion.

In Ontario a DUE Pharmacy Specialty Group has been formed with antibiotic use being a major focus. They meet every month or two with a more formal agenda consisting of speakers and an opportunity to compare experiences. The University Health Network (UHN) and Mt. Sinai Hospital in downtown Toronto have a joint cardiovascular subcommittee, which evaluates relevant new medicines, however the recommendations are presented to 2 separate PTCs often with very different results. This is in part due to the different financial and organizational structure of each institution.[28]

Representatives from hospital pharmacies across Canada have indicated a significant level of concern regarding the rate at which in-hospital drug costs are increasing. Several suggestions were made acknowledging the necessity for more collaboration in both the public and private sectors at the provincial and the national level. Duplication of effort is often seen as a waste of precious resources, and more streamlining of the drug evaluation and formulary management processes could allow those resources to be used much more effectively. Another suggestion was made to treat new hi-cost drugs as a capital expenditure just like any new hi-tech tool. This is a similar approach to that taken by the UK in the formation of NICE.

In order to deal with this problem, perhaps new and expensive drugs should be treated somewhat like a capital expenditure. The new drug would have to be specifically funded by government before it was allowed to be used in the hospital setting. Drugs would then have to be justified like a new NMR machine, or a new CAT scanner, and would presumably have to be prioritized high enough to successfully compete for any new funding for health care that the government made available.[29]

Section II. Experience With Centralized Hospital Formularies: Two Models

A. QUEENSLAND, AUSTRALIA

Context

Located on the northeast coast of the continent, Queensland is Australia's second largest and fastest growing state, covering an area of over 1.7 million square kilometers (roughly 25% of the continent's land mass) and inhabiting about 3.5 million people. By comparison, Ontario covers 1 million square kilometers and has a population of about 11 million.

Queensland Health operates about 150 public hospitals in 38 Health Service Districts. These range from an 850-bed tertiary referral hospital in Brisbane to smaller provincial referral centres along the Gold Coast (e.g., in Rockhampton, Townsville, and Cairns) to a host of outpost hospitals such as Quilpie Hospital, which is located 1,000 km west of Brisbane, serves a population of about 600 people, has ten beds, and is staffed by a team of nurses and one physician. Forty (27% of) hospitals have at least one full-time pharmacist.[30]

Queensland public hospitals are state funded to a significant extent using Commonwealth-provided funds in accord with agreements between the state and the Commonwealth (federal government). Among other things, these agreements require the state to cover (with few exceptions) all treatment costs, including both in- and out-patient medicines. Hospital out-patients contribute a co-payment for medicines (about AU$20 per item for general patients and about AU$3.60 for pensioners and other concessional patients) comparable to that charged by the Commonwealth-funded PBS which supplies most out-patient medicines prescribed by general practitioners and specialists in community-based private practice.[31] With the exception of drugs covered under a separate, Commonwealth-funded "High Cost/Highly Specialized Drugs (HSD)" funding program (see below), medicines prescribed by hospital-based physicians are paid for by the admitting hospital's global budget. In the year 2000, about 4% of Queensland hospitals' total operating expenses (AU$3.3 billion) were spent on drugs.[32]

Standard Drug List (SDL) for Queensland hospitals

Originally established in 1973 by the Brisbane Hospitals Drug Advisory Committee, the SDL now serves as the central formulary for all Queensland public hospitals, contains about 950 chemical entities, and is managed by the broadly representative Queensland Hospitals Drug Advisory Committee (QHDAC). (See below for more on QHDAC.) Where they exist, hospital- or district-level PTCs typically address local policy issues, review requests for additions to the SDL before submission to the QHDAC, and set local procedures and protocols for such things as stockholding.

A primary motive for establishing the SDL was Queensland Health's belief that a statewide formulary would limit duplication of effort and resources, and would facilitate equity of access.[33] A sample extract can be found in Figure 5, Appendix V. Products approved for use are listed in three columns: the product name, form and strength; the number of units in a standard pack; and any restrictions placed on the product's use. The aim of these restrictions is to encourage safe and cost-effective prescribing by controlling the availability of new drugs until there is satisfactory local experience with their efficacy and toxicity, and by limiting the availability of expensive items to treat specific diseases, which cannot be managed by other more economical or well established drugs.

Where applied, these restrictions fall into four main categories.

- Specialist Staff - The drug will be available at the direction of Specialist Staff only.
- Specialist Staff or Medical Superintendent (Chief of Staff) .
- Only on the advice of an Infectious Disease or Clinical Microbiology Specialist– to minimize the development of antibiotic resistance.
- In accord with Highly Specialized Drug (HSD) Program indications. [See below.]

Where individual patient clinical need requires the use of a non-formulary drug, approval may be granted by the hospital's Medical Superintendent or the QHDAC.

Requests for additions to the SDL are typically made to the QHDAC by a staff physician through his/her Medical Superintendent with approval from the hospital's Director of Pharmacy and/or PTC, where applicable. Requests from pharmaceutical manufacturers are not considered. However, in practice, the standardized submission document is frequently either based upon or accompanied by pre-prepared documentation supplied by manufacturers.[30]

While the submission must meet some basic informational requirements, supplementary materials typically include:

- evidence of efficacy and toxicity from published Phase I, II, III, and IV studies;
- comparisons with alternative drugs including cost comparisons and evidence from published studies of head to head trials;
- estimates of numbers of patients and of cost impact at hospital and statewide levels; and, where therapeutic alternatives are available on the SDL,
- evidence that the new product is at least equally efficacious, more cost-effective, or less toxic than existing drugs.

Consideration also is given to avoiding unnecessary duplication of like drugs on the SDL. The application form also includes a declaration of potential conflicts of interest.

Queensland Hospitals Drug Advisory Committee (QHDAC)

The main purpose of the QHDAC is to advise the Director-General (through the General Manager, Health Services) on the selection and appropriate use of therapeutic substances to be made available in Queensland public hospitals. It is Queensland Health's belief that a statewide approach not only avoids duplication and ensures even access, it has the potential to minimize the influence of biases that are more likely to affect formulary decisions made at a hospital level.

The committee's broader mandate is fulfilled by providing several functions:

- reviewing applications for products to be added or deleted from the Queensland Hospitals SDL, identifying conditions/restrictions for use, and maintaining that list;
- considering the cost-effectiveness of products used within the hospitals; (For expensive drugs, the committee compares cost-effectiveness of a new agent to existing therapies and decides what restrictions, if any, should be placed on its use.)
- identifying any products recommended for listing which may have substantial budgetary implication for Queensland Health;
- advising on the suitability of alternative drugs offered on tender to the State Government both in relation to their pharmacological and pharmaceutical properties and costs;
- monitoring usage of selected drugs at hospital and state levels, and encouraging appropriate use;

- advising on problems related to therapeutic substances which are raised by the staff of Queensland Health or its hospitals/institutions;
- encouraging and supporting development of effective drug PTCs at the hospital level;
- encouraging Adverse Drug Reaction reporting;
- liaising with Commonwealth authorities and manufacturers where decisions on products affect their availability in Queensland public hospitals/institutions;
- maintaining a system whereby urgent approvals can be given for drugs or indications not listed on the SDL;
- maintaining a process to deal with potential conflicts of interest;
- taking an active role in ensuring responsible promotion of drugs listed on the SDL; and
- encouraging benchmarking of performance of the QHDAC.

Throughout the years, the QHDAC has typically involved 12-15 members chosen for their recognized expertise, rather than for their hospital affiliations or areas of practice. Currently, members include a general practitioner, anesthesiologists, clinical pharmacologists, a hematologist, a psychiatrist, an oncologist, a pediatrician, an infectious disease specialist, two clinical pharmacists, and administrative/clinical support.[30] In almost all cases, the clinicians have a current practical clinical caseload.

The QHDAC also operates two standing subcommittees (Infectious Disease (which advises on proposed anti-infective listings and provides advice for the publication of Antibiotics Guidelines) and Dietetics & Nutrition) and a Specialist Panel. The Specialist Panel is a group of external experts, any of whom may be invited to attend QHDAC meetings for discussion of particular topics. Other sub-committees are struck as needed and, where possible, are chaired by a member of QHDAC. In addition, the committee will frequently write to other specialists for input on a new product's "anticipated place in therapy".[30]

Minutes of QHDAC meetings and committee recommendations are sent to the General Manager (Health Services) for approval and, once approved, pharmacies and relevant officers in Queensland hospitals are notified of any revisions to the SDL. These updates are then circulated within the hospitals to inform professional staff.

High Cost/Highly Specialized Drug (HSD) Funding Program

Originally established in 1991 to help states with rising costs associated with the use of cyclosporin, erythropoietin, and later, drugs for HIV/AIDS, this federally-funded program currently offsets Queensland Health's prescription drug costs by about AU$40 million annually.[30] The currently covered products are listed in Figure 7, Appendix V.[34]

Criteria for coverage include:

- market approval in Australia for approved indications;
- ongoing specialist medical supervision;
- an identifiable patient target group;
- treatment for a chronic medical condition (as opposed to acute episodes of in-patient treatment (This does not preclude day patient administration.)); and,
- high unit cost.

Further, the Commonwealth Government will pay the agreed price, above the patient standard contribution, for each issue of a covered medication provided:

- it is supplied by an approved hospital pharmacy;
- recipients are patients in the community or attending day services (i.e., not in-patients) and are eligible to receive medication through the Public Hospitals system;
- documented usage information (for the covered drugs and approved indications) is provided by the state on a quarterly basis (See Figures 8 & 9, Appendix V for a sample report.[34]);
- prescriptions are according to agreed Pharmaceutical Benefits Advisory Committee criteria; and,
- states can satisfy the Commonwealth that adequate and auditable systems are in place to verify that above conditions are being met.

To comply with the last condition, Queensland Health has established an audit process to test the validity of claims to the HSD Program. This includes an audit by a member of the submitting hospital's staff (preferably a pharmacist) of a 3% (under review) random sample of hospital medical records to confirm that each drug claim relates to the approved indications. To be eligible for reimbursement, each initial prescription for a covered drug must be accompanied by a completed Form E2 (See Figures 10 and 11, Appendix V for a sample). These forms are retained by the hospital pharmacy for statistical purposes and provide the population from which the 3% random sample is drawn. Hospitals' quarterly submissions to Queensland Health must indicate that this audit has been done.[34] An overview of the reimbursement process is provided in Figure 12, Appendix V.

Decisions about which drugs are covered under the HSD Program are made by a national working party with representation from each state's health department and the federal government. In short, this group makes its recommendations by considering proposed drugs against the above five basic eligibility criteria and (quality, safety, efficacy, and cost-effectiveness) criteria established by the Commonwealth's PBAC; the committee that advises on drugs for inclusion on the national formulary (the PBS).[30]

B. WINNIPEG REGIONAL HEALTH AUTHORITY (WRHA)

Context

Established in 1999, the WRHA is one of twelve Regional Health Authorities in Manitoba. With an annual budget in excess of $1 billion it supplies the health care needs to over 600,000 people, more than half the Manitoba population. The WRHA, which includes four community hospitals, two tertiary hospitals, three long term care health centres, 37 personal care homes, and 16 community health offices. [35]

Prior to the formation of the WRHA, the great disparity in the approaches of its individual facilities to formulary management likely reflected the uncertainty amongst pharmacists and physicians as to what constituted a good formulary system. The WRHA is looked upon by the province's rural health regions as a leader in hospital formulary management. [29]

Regional PTC

Although in Manitoba formulary management is now largely done on a regional basis, discussions are ongoing about a possible single province-wide formulary process. In the meantime, a significant degree of standardization has already been reached by cooperation between regions, and WRHA's contracting program now serves the other regions as well. The WRHA PTC itself is largely a policy making group that deals with the major issues passed to it by the subcommittees that do most of the work and make most of the decisions. At present the subcommittees of the PTC include:

- adult pharmacotherapy,
- pediatric pharmacotherapy,
- oncology,
- anesthesia,
- long term care pharmacotherapy,
- medication administration policy,
- medication error,
- formulary, and
- medical devices.

The adult, pediatric, oncology, anesthesia and long term care subcommittees that make recommendations concerning formulary status attempt to evaluate the cost/benefit of new drugs in different patient subgroups based on the available evidence in the literature. In general this takes the form of restrictions on the use of new drugs, however, difficulties frequently arise in the subjective assessment of the relative value of a particular drug benefit.

The Process

The move to a central regional PTC along with other changes associated with regionalisation has been a significant challenge for the individual institutions, however, the magnitude of the cost and resource issues involved with formulary management has supported this approach. Most facilities no longer have a PTC, although some have a committee, which facilitates implementation of the regional formulary decisions. In the process of developing a central formulary, new drugs have been the most straightforward, whereas the 3000 existing drugs on the 9 facility formularies have not. This latter drug group has not yet been completely reviewed, so although most standardization decisions have been made, a final complete formulary has not yet been released. Attention directed towards a well maintained formulary in electronic format has revealed resource problems for the WRHA, and the differences between acute and long-term care has necessitated the creation of a long-term care subcommittee. [29]

Approaches to Managing High Cost Drugs

Very expensive new drugs are the main reason for concern about hospital drug costs which are increasing at a much greater rate than are government funded hospital global and drug budgets. As a result, in order to stay within the drug budget, hospitals must cannibalize some other services to fund new drugs, or decide not to use those products. The latter approach has been the primary means of controlling drug expenditures within the WRHA pending resolution of funding issues with the provincial government. [29]

In its efforts to control drug costs, the WRHA strives to balance organizational efficiency and patient welfare as revealed by these objectives:

- Major restrictions on drug availability and use will apply only to agents with a narrow therapeutic index, that are complicated to use, that are more expensive than effective alternatives, or that have an impact on microbial ecology.
- More flexibility and individualization will be permitted as patients move from outpatient to inpatient care with primary agents defined and promoted as the drug of choice for initiating therapy or as an alternative for therapeutic interchange whenever appropriate. One of the major criteria for selection of a primary agent will be its availability on formularies in the outpatient setting. This desire for consistency between in- and out-patient formularies has been quite successful. One of the regional PTC members also sits on the provincial formulary panel, the Drug Standards and Therapeutics Committee.
- Care maps and drug-use criteria, rather than non-formulary status, will be primary tools for managing drug utilization.
- Non-formulary status will apply to drugs that have been rejected, removed or not yet evaluated by the PTC, and will be supplied only with approval of the relevant subcommittee.
- The regional practice model for staff pharmacists will include responsibility for both patient-care and drug-use management aided by educational interventions involving physician, pharmacist, and patient.[36]

Plans are underway to study the cost-effectiveness and patient care implications of these changes.

External Funding

The supplements for drug budgets that were in place in the past were primarily for outpatient drugs that were being supplied to outpatients at no cost, as part of what is usually referred to as the "hospital-insured" outpatient drug program. That program is being transitioned from hospitals to private sector pharmacies, largely as a result of pharmacist manpower shortages in Manitoba hospitals that have forced hospitals to focus their pharmacist manpower on inpatient services. The program is expected to be run through Pharmacare, using the provincial pharmacy claims network to manage the program.

Regarding medications such as infliximab given in hospital to outpatients, the WRHA, like Saskatchewan and many facilities across the country, has interpreted the Canada Health Act such that only medicines required as part of outpatient procedures will be covered by the hospital, pending an explicit government solution for this issue.

The WRHA believes that the government must provide new funding for expensive new inpatient drugs. ‘Expensive’ is defined as adding more than $20,000 in incremental costs annually to the region. It was proposed that government either provide a new drugs "pot" of funding, equivalent to 10% of the previous year's drug budget, which the WRHA would manage or that government would approve the funding for each new drug first. Since neither option has yet happened, these medicines will not be generally available to inpatients until a specific funding method is provided by government. [29]

SECTION III. Financial Considerations for OCOTH Hospitals

Introduction

Given the rapid transition from inpatient to outpatient provision of health care services over the past decade, the changing population demographics towards an older community, and the continuous technological progress in health care, much attention has recently been given to drug utilization and expenditures in Canada. While total health expenditures in Canada were estimated to have increased from $39.9 billion to $84 billion from 1985 to 1998, representing an increase of 111%, expenditures on drugs in Canada were estimated to have increased from $3.8 billion to $12.4 billion, an increase of 227% during the same time period[6]. Drug therapy is the fastest rising and second largest constituent of health care expenditures, representing nearly 16% of total health care expenditures in Canada[37].

The nature of health care expenditures at the hospital level may be substantially different from that at the non-hospital level. Contextually, restructuring and downsizing in the hospital sector has led to 23% fewer hospital beds in the health care system between FY 1993 and 1997[37] is observation may be contributing to the improving financial health of hospitals in Ontario in recent years. After adjusting for population growth, hospital revenues have generally increased by approximately 10% as hospitals debts decreased slightly from FY 1997 to FY 1999 [38]. Hospital expenditures per patient as well as drug expenditures per patient appear to have increased as well. Although bed reductions were offset to some degree by reductions in length of stay and substituting outpatient care for inpatient stays, data from the Canadian Institute for Health Information (CIHI) suggest a shift in drug expenditures from hospitals to the community[37]. Relative to the inpatient environment, this may pose increased financial pressures on public and private payers.

In accordance with these observations, while significant increases in drug expenditures have been documented for outpatient drugs, studies generally suggest relatively less substantial increases in inpatient drug expenditures. For example, the Ontario Drug Benefits Program has reported drug expenditures to increase by approximately 50% over the five-year period from 1995 to 2000 and public expenditures on medications by the government in Ontario now stand at approximately 16% of all government health care expenditures. In contrast, inpatient drug expenditures have increased by approximately 20% during this same time period and have been estimated to account for less than 4% of total hospital expenditures[6]. It is also acknowledged, however, that smaller hospitals may be very different from larger academic centres in their drug utilization and expenditures and aggregate estimates may not be generalisable to all hospitals. A current snapshot of drug expenditures in OCOTH hospitals would be helpful.

SURVEY OF FINANCIAL INDICATORS FOR OCOTH HOSPITALS

Methods

OCOTH member hospitals agreed in principle to participate in a self-administered electronic survey to assess drug-related expenditures at the respective hospitals and granted ICES permission to contact their pharmacy directors. Each prospective subject received a copy of the survey instrument by mail and electronic mail, accompanied by a brief introductory letter signed by the study investigators and a promise of telephone or electronic mail follow-up to answer any questions about the survey and to arrange a time

to complete a second interviewer-administered questionnaire to examine PTC structure and function. A copy of this first survey is attached in Appendix VI.

Findings

While all 16 OCOTH hospitals agreed to participate in this survey, 1 hospital was unable to complete the survey given data limitations. One additional hospital returned a relatively unfinished survey, rendering its reporting unusable, leaving 14 surveys available for analysis. The quality of reporting was highly variable with many fields left incomplete. Consequently, many of the estimates derived from this survey are based on a limited number of hospitals. While it is acknowledged that different hospitals will have different patient volumes and mixes of patient care services and will deliver different types pharmacy services, the small number of adequately completed surveys precluded us from conducting subanalyses taking some of these factors into consideration. Most of the findings are presented as aggregate estimates for all responding hospitals.

Financial estimates were requested for FY 1998-2000. Hospital expenditures increased by approximately 26% over the three years assessed whereas hospital admissions declined by 2%. (Table 24, Appendix VI) The ranges of values for these estimates are reasonably wide, indicating large variability between years and hospitals. All hospitals reported increasing total hospital expenditures between 1998 and 2000 whereas 70% of respondents reported decreases in total number of hospital admissions during the years assessed. The total hospital expenditure per admission increased by approximately 29%. While overall total drug expenditures were reported to increase by approximately 19% over the three years assessed, two-thirds reported consistent increases in total drug expenditures over the years assessed. Total drug expenditures accounted for approximately 4.3% of total hospital expenditures. This estimate ranged from 2.2% to 7.6%. Approximately 75% of reporting hospitals experienced decreases in the proportion of total hospital expenditures attributable to drugs. The average relative reduction in drug expenditures as a proportion of total hospital expenditures was modest at 1.4% (range 24% decrease to 56% increase). Approximately one-third of total drug expenditures were covered by external sources such as rebates and funding from the Ontario Ministry of Health (range 4.5%-66.3%). An average increase of 46% in external funding was also observed during the time period (range decrease by 37% to increase by 142%). The average net annual drug expenditures (i.e. total drug expenditures excluding external funding) as a proportion of total health expenditures for reporting hospitals was estimated to be 2.8% and ranged from 1.5% to 4.2%. No significant differences were observed between the different hospitals and their acquisition costs of the drugs of interest given their enrolment in common provider plans.

Interpretation

The pressures facing the outpatient environment appear to outweigh those facing the inpatient environment. However, the availability of extremely high cost drugs may pose substantial and unexpected increases in overall drug expenditures yet they may also provide substantial clinical benefit. For example, the recent introduction of glycoprotein 2b/3a inhibitors has resulted in nearly 10% of all drug expenditures to be dedicated to this class of drugs in some hospitals. The clinical benefit of these medications in patients undergoing coronary stenting has been demonstrated in numerous clinical trials. Funding from government sources has been required and provided to supply this class of drugs.

GOVERNMENT SOURCES OF FUNDING FOR ONTARIO HOSPITALS

Special Drugs Program

The Special Drugs Program (SDP), which covers drugs listed under Section 8, Regulation 552 of the Health Insurance Act (Appendix IV), is restricted mainly to rare or life-threatening conditions for which drug therapies have traditionally been costly. Among them are enzyme deficiencies, such as Gaucher's Disease (alglucerase), endogenous growth hormone deficiency, thalassemia, cystic fibrosis, and HIV/AIDS. Other costly therapies adopted by the SDP include cyclosporin for patients undergoing solid organ or bone marrow transplants, erythropoietin for patients with end-stage renal disease, and clozapine for treatment-resistant schizophrenia.

The SDP is administered by the Ontario Drug Benefit Program (ODB) of the Ontario Ministry of Health. The last time a drug was adopted by the SDP was 1993, and others were introduced at various times for various reasons. For example, several drugs, such as alglucerase (for Gaucher's Disease), were originally administered through hospital-based programs, but were later transferred to the SDP. Accordingly, with the exception of Cystic Fibrosis therapies, few if any of the covered therapies were subjected to a formal review and approval process.[39] Currently, hospitals administering covered therapies are reimbursed on a cost recovery basis through the SDP, and for specific drugs (cyclosporin, human growth hormone, and medications for cystic fibrosis and thalassemia) only pre-approved hospitals are paid (Tables 20 and 21, Appendix IV).

A recent provincial audit of the SDP recommended not only that the Program not be expanded, but also that strategies for dissolving it be explored.[39]

Cancer Care Ontario's (CCO) New Drug Funding Program

Program Overview

CCO's New Drug Funding Program was established in 1995. The goal of the program is to provide equal access to new effective agents for eligible patients throughout the province. As a result, access to expensive drugs is not limited by place of residence or by a health care facility's drug budget, and new treatments are introduced in a standard manner on a provincial basis. Prior to 1995, all intravenously administered (IV) anti-cancer and supportive care drugs were paid for out of the global budgets provided to hospitals and cancer centers as part of negotiated annual allotments from the Ministry of Health. And the decision to provide these therapies and to pay for them was the responsibility of the individual institutions rather than CCO.

A Policy Advisory Committee (PAC) recommends to CCO the drugs and the eligibility criteria for funding, after reviewing Evidence-based Guidelines that are developed by eleven multi-disciplinary provincial disease site groups that are part of the CCO Program in Evidence-based Care. CCO is responsible for managing the Program's budget on behalf of the Ministry of Health, and reimburses cancer centres and hospitals for the costs of approved medications for patients who meet pre-specified eligibility criteria. (A sample reimbursement form is attached in Figure 4, Appendix IV.) During 2000/2001, the New Drug Funding Program had a budget of 37.5 million and funded 14 drugs for 24 indications.[40] The currently funded drugs are listed in Table 22, Appendix IV.

History, Role, Composition, and Procedures of the Policy Advisory Committee (PAC)

In 1994, a CCO (Systemic Therapy) Task Force was formed to explore ways in which to resolve problems of uneven access to cancer therapies across the province. The task force, which included health professionals (physicians, nurses, and pharmacists), community representatives, and a health economist, met over several months during that year and prepared a report to the Ministry of Health. Accepting its recommendations, the Ministry instructed CCO to implement a centralized funding system for newly approved IV drugs (the New Drug Funding Program); and, in turn, responsibility for recommending which drugs to fund and under what conditions was given to a Policy Advisory Committee (PAC). Currently, the PAC meets 2-3 times per year and has a composition similar to that of its parent task force: 3 lay members (including 1 patient); a government representative; a pharmacists; a nurse; 2 administrators; and 7 oncologists (1 of whom is Director of CCO's Practice Guidelines Initiative). Replacements are appointed by a Vice-President of CCO in consultation with the Chair of the PAC.

Ideas for additions to the New Drug Funding Program come from various sources (e.g., PAC members, Chairs of CCO's Practice Guidelines Initiative (CCOPGI) Disease Site Groups, drug manufacturers, etc.). However, no drug is considered by the PAC without first being reviewed by the appropriate Disease Site Group of the CCOPGI. (Although the PAC was originally envisioned as fulfilling a much broader role, complementary to the CCOPGI; to date, the PAC has been confined to issues related to the New Drug Funding Program.[41]) These reviews take one of two forms. In situations where data from randomized controlled trials exist, the relevant CCOPGI Disease Site Group develops a full Clinical Practice Guideline Report, complete with firm recommendations for use. When such data are lacking, the CCOPGI prepares an "evidence summary" which also synthesizes the research evidence, but restricts interpretation of the evidence to opinion-based statements that fall short of formal clinical recommendations. Typically, such reports are accompanied by an "evaluation matrix" completed by the Secretary of the PAC in consultation with the drug's manufacturer and the Chair of the Disease Site Group.[42] A sample evaluation matrix is attached as Table 23, Appendix V.[41]

While drug cost projections are considered by the PAC, to date, formal cost-effectiveness or cost-utility analyses have not been used for several reasons:[41]

1. The PAC has tended to use a threshold approach to decisions in which evidence of benefit and quality of evidence have been considered before cost. However, cost has influenced the conditions under which a drug is to be used or how carefully it is to be monitored.
2. To date, requests for additional funding for approved drugs have been granted by the Ministry of Health and Long-term Care.
3. As the New Drug Funding Program has responsibility only for drug acquisition costs, other potential financial benefits or costs that might accrue with a given therapy have reportedly been difficult to incorporate into listing decisions.

Reflections on the PAC

Recently, Pater et al. made some observations based on their personal experience with the PAC:[41]

1. A major challenge for the committee has been the evaluation of drugs for which the best evidence comes from non-comparative (phase II) trials in which the only outcome measured is tumour response. Achieving consensus on denying products that show promise in phase II studies has been particularly difficult when there are few if any treatment alternatives. (Reportedly, such therapies have been approved by the PAC on a conditional basis, with funding contingent upon the monitoring and reporting back of rates of response to therapy.)
2. Community representatives make important contributions to ensuring that the approval process is transparent and fair.
3. The PAC's ongoing need for timely access to high-quality information has led to delays for other important initiatives of the CCOPGI.
4. Concerns exist that, in the long term, it may be difficult for CCOPGI reviewers to remain unbiased in their judgements about products they know will ultimately be considered by the PAC.

INDEPENDENT LEGAL INTERPRETATION OF THE CANADIAN HEALTH INSURANCE ACT

Funding of Drugs Provided in Outpatient Clinics Located in Hospitals

The issue of funding of drugs used in hospital outpatient clinics is extremely controversial. While some hospitals fund use of medications in this setting through the global budget, others insist that third-party payers should cover these drugs since many patients visit an outpatient treatment program solely for the purpose of administering a drug. Consequently, these differences may result in uneven access to some therapies.

An independent legal opinion regarding the financial responsibility for drugs administered in outpatient clinics indicates that, with some exceptions, neither the hospital nor any specific branches of the MOH are legally responsible if the sole purpose of the visit is for the administration of medication. This argument illustrates the problem with silo funding, since all Ontario hospitals are ultimately funded by the MOH and therefore hospitals should not be viewed as entities independent of the MOH in this regard. (See Appendix IV for details.)

SECTION IV: Drug Management in OCOTH Hospitals

Introduction

When evaluating the value of a particular intervention, the magnitude of the clinical benefits must be weighed against the magnitude of financial investment since limited resources may be best directed at interventions that maximize outcomes at minimal costs. Treatments cannot be proven to be of value themselves, however. They can only be of value for a particular indication or population in relation to a defined alternative [43]. The inclusion of a high cost, potentially high impact drug warrants careful scrutiny with significant expertise in both the clinical and economic realms. This necessarily warrants examination of the hospital drug approval decision-making process.

Methods

Using a telephone survey, we examined hospitals' PTC compositions and policies and procedures for selecting, purchasing, monitoring, and re-evaluating medications listed on the formulary. The survey focused on six domains in the formulary process, namely pharmacologic and clinical evaluation, pharmacoeconomic evaluation, development of drug use criteria, administrative and ethical issues, drug use monitoring, and follow-up review [44]. One of two ICES Research Coordinators conducted a 60-90 minute telephone or face-to-face interview (Appendix VI) with each of the 16 OCOTH hospital pharmacy managers. The interview focuses on the hospitals' P & T committee composition and policies and procedures for selecting, purchasing, monitoring, and re-evaluating medications listed on the formulary. As well, we sought subjects' opinions about the feasibility, composition, and role of a proposed centralized OCOTH PTC. Where possible, these responses were supplemented by other Committee documentation, such as terms of reference and forms used to request changes in formulary status or to declare conflicts of interest.

The survey was reviewed by two OCOTH pharmacy directors for clarity and comprehensiveness prior to conducting the survey. However, neither were subjected to formal pilot testing or validation work. The research protocol was approved by a Research Ethics Board at Sunnybrook & Women's College Health Sciences Centre, Toronto and was supported by an arms-length grant from OCOTH.

Findings

According to subjects, all of the hospitals operated a PTC with a primary responsibility for recommending what and how drug therapies should be used at the hospital. All respondents were members or former members of those committees and judged themselves qualified to report on the committee's composition and procedures.

Committee size ranged from 11 to 30 standing members (mean (SD): 16.5 (5.9), median: 16). In general, multi-site hospitals tended to have larger committees, and the committees from long-term care and rehabilitation facilities were smaller. All had medical, pharmacy, and nursing representation. Less common was representation from senior-level administration (9), house staff (3), quality or risk management (3), clinical pharmacology (3), or nutrition (2). Two committees had at least one standing member with advanced training in health- or pharmaco-economics, and 2 others reported having access to and using such expertise as required. Just one committee reported any involvement of an ethicist.

In addition to having medical representation from most if not all hospital programs, seven subjects also reported the existence of standing subcommittees that could be called upon to provide clinical or methodologic expertise in areas such as infectious disease (5), cardiology (3), and oncology (2).

Procedures for reviewing therapies for addition to the hospital formulary

Here, we asked subjects to consider their review procedures under two conditions: one in which a drug under consideration would result in a high cost burden to the hospital (i.e., >10% of the hospital's drug budget); and another in which the cost impact, by comparison, would be relatively low (<1% of the drug budget). Elements common for both scenarios and to virtually all hospitals were: the preparation of a standardized review document for consideration by the committee; involvement of at least one pharmacist, one physician (most often the requestor), and routinely other clinical advisors or committees in preparing the submission; distribution and formal presentation of the submission to the committee by at least the requestor (and frequently one other individual, usually the pharmacist); notification of the requestor of the PTC's recommendations and opportunity for challenge; ratification by the hospital's Medical Advisory Committee; and notification of the hospital staff. This process is summarized in Figure 13, Appendix VI. In general, the safety and efficacy of and need for a drug are the Committees' primary considerations. Once these are established, only then would most of the committees consider economics.

Less frequently cited features or elements restricted to evaluations of high cost-burden therapies (reported by 9 (56.3% of) subjects) were: routine tracking of non-formulary drug utilization as a trigger for the PTC consideration (3 (18.8%)); use of explicit criteria to grade the strength of evidence or recommendations for a therapy (4 (25.0%)); "regular" input from standing subcommittees for clinical advice (7 (43.8%)); routine input from individuals with advanced training in health- or phamaco-economics (5 (31.3%)); regular review of relevant decisions taken by other PTC or formulary review committees (1 (6.3%)); and explicit dollar thresholds for Program and/or senior administrative approval (4 (25.0%)).

After considering the evidence, all of the committees reportedly face four basic decision options: request more information; list the product; list the product with conditions; or do not list the product. The most commonly reported conditions were time-limited listings (with accompanying requirements for utilization reviews) and restrictions by indication or service. Typically, such restrictions would be proposed in the submission and would be discussed and agreed to at the time of approval, along with any recommendations for how the restrictions should be monitored or enforced. Examples included pre-printed orders, requirements for the pharmacy to review orders, or drug utilization reviews.

Reflecting on the above, each subject was asked to make judgements about his/her committee in two areas: i) the level of care taken by the committee in evaluating new drug therapies; and ii) the level of confidence they have in the personnel responsible for collecting and appraising evidence regarding the effectiveness and cost-effectiveness of these therapies. Their responses are summarized in Tables 25 and 26, Appendix VI. In sum, ratings of "care" were more variable for low as compared to high cost-burden therapies, and levels of confidence in reviewers' abilities to find, appraise, and understand the relevant evidence varied considerably.

One perceived obstacle to greater consideration of cost-effectiveness data was a prevalent incapacity on the part of member hospitals to both effectively track and share financial savings that might accrue outside the drug budget (e.g., as a result of reduced drug administration time, other nursing time, operating room

time, length of stay, etc.). This was perceived to be less of an issue among respondents whose drug budgets were functionally decentralized. Although, even here, such offsets were rarely if ever formally tracked. Another common complaint was the variable quantity and quality of evidence available to the committee for economic evaluation.

Procedures for disclosing conflicts of interest

If it were discovered that a PTC member has presented materials on a drug under consideration on behalf of its manufacturer in the past several months, how would this situation be handled?

This scenario prompted six (37.5% of) subjects to describe their formal, written policies for disclosing conflicts of interest; four of which would permit the affected member to participate in committee discussion, but would exclude them from decisions. In the other two hospitals, the affected member would be permitted to participate in both discussions and decision-making. All other respondents believed that it was worthwhile to have such policies, and most planned to develop one in the months ahead. Other situations that subjects felt might warrant disclosure included serving as a consultant to a drug manufacturer, participating in clinical trials carried out by the manufacturer, and receiving research grants from a manufacturer.

Strategies for monitoring utilization, containing costs

Table 27, Appendix VI lists the strategies reported. While all were judged to be useful and effective to varying degrees, subjects claimed that resource limitations (both financial and human) prevented their broader and more consistent application. Unit-based pharmacists were perceived to be one of the more effective strategies, and virtually all respondents wished for greater access to such resources. Two centres also reported high hopes for systems for physician order entry and case costing that would permit lower, drug-level analyses. Other perceived challenges were the enforcement of dosing protocols and clinical practice guidelines, the timeliness of order review (particularly at night and on weekends), and an inability to truly "manage" formularies due to a need to accommodate incoming patients' long-term therapies.

A separate but related issue raised by several subjects was a lack of accountability for drug expenditures at the hospital Unit, Department, or Program level. For several hospitals (5 reported here), at least part of the institution's drug budget was functionally decentralized. Some respondents believed this helped motivate Programs to take greater interest in efforts to monitor utilization and contain cost. One reported trade-off is the potential for added administrative burden for staff at the Unit level.

See Appendix VII for a review of the evidence for strategies to improve prescribing in the hospital setting.

Integrating new formulary listings into the budget-setting process

Few hospitals had formal mechanisms for this. One option that was available to several PTCs was a "conditional" time-limited (6- or 12-month) listing, during which drug utilization and expenditures (and sometimes outcomes) would be tracked and reported back to the Committee for consideration of the product's ongoing status on the formulary. While all believed this to be a useful tool, most questioned the feasibility of its broader application given current staffing levels. More common strategies were requests for budget impact analyses (most often projections for annual utilization and costs) at the time of application for listing, and annual reviews of expenditures for the hospitals' most expensive therapies,

typically the top 25 or 50 agents. As described above, in some cases, cost projections also triggered the involvement of experts in pharmacoeconomics or senior administrators to assist in listing or monitoring decisions. Several subjects commented on the challenge of making accurate projections for some drug products (as compared others, such as in surgery, anesthesia).

Other utilization management strategies were employed to varying degrees, based on, among other factors, the projected cost of the agent to the drug budget and the capacity to track costs at the drug/patient/Unit level and/or the extent of functional decentralization of the hospital drug budget. For a few institutions, periodic variance reports at the Unit or Program level served as triggers for closer inspection.

Purchasing and funding in-hospital drug therapies

All but one hospital (93.8%) used a group buyer/negotiator to acquire at least some of its lower-cost, higher-volume mostly multi-source drugs (9 HealthPro, 6 MedBuy). However, the scope of coverage was considerable, ranging from an estimated 25% to roughly 75% of "line items". Several hospitals also cooperated on the purchase of some lower-volume, higher-cost agents, such as anti-infectives, injectibles, and glycoprotein inhibitors. Typically, very low volume or specialty items were purchased through hospital-specific contracts with manufacturers. However, most expressed having limited success in achieving meaningful price reductions on other than multi-source products. Further, several respondents expressed frustration over manufacturers' increasing efforts to 'bundle' products (i.e., discounts for products that are dependent on the purchase other products or services). Two subjects also mentioned obtaining unapproved medications through Health Canada's Special Access Program. While all subjects acknowledged that some variation in acquisition costs was likely, none judged it to be large or very important.

For all OCOTH hospitals, the primary funding source for in-patient drug therapy is the hospital's global budget. These expenditures are off-set to varying degrees by other special funding programs for specific diseases, drugs, or disease-drug combinations (e.g., Cancer Care Ontario's (CCO) New Drug Funding Program, Ministry of Health and Long-term Care's (MOHLTC) Special Drugs Program, Cardiac Care Network (CCN) funding for glycoprotein 2B/3A inhibitors) based upon the hospital's clinical programs or patient mix. For example, whereas one OCOTH hospital may receive virtually nothing from these special funding programs, for another these sources may cover over half of the hospital's annual expenditures on drugs.

Opinions about the role, feasibility of a proposed centralized PTC

The notion of a centralized committee and review process for high cost-burden drugs drew a range of reactions; however, most fell into three broad categories. Four (25% of) respondents were either pessimistic or skeptical about its feasibility (without additional funding) or expressed a need for more information. Without such information, most (9 (56.3% of)) respondents were willing to at least consider the idea and saw its merits (in terms of equity, improved efficiency and quality of reviews, etc.). However, without additional funding, these subjects also expressed grave concern about being bound to the Committee's recommendations. Three subjects (18.8%) believed that Cancer Care Ontario's (CCO) New Drug Funding Program could serve as a model for moving discussions forward on this proposal. In their view, key elements for success would be: tying Committee approval to centrally-administered reimbursement for patients meeting pre-specified criteria; access to the program by all Ontario hospitals;

and mechanisms and capacity for program audits. Among the more frequently cited examples of drugs this committee could consider were glycoprotein 2B/3A inhibitors, remicade, liposomal amphoB, and activated protein C.

Among the perceived advantages of a centralized review/approval process were: improved efficiency and quality/calibre of reviews; greater potential for taking both a hospital and a broader/population/societal perspective when considering cost-effectiveness; equity of access to proven therapies; a potential role for the committee in price negotiations; and the potential for financial support to off-set the rising cost of in-hospital therapies. Among the perceived challenges were: developing processes that will ensure fair representation of relevant constituencies (hospitals, clinical areas, programs, etc.) in decision about what drugs are considered, committee membership, etc.; the timeliness/responsiveness of the decision-making process; protection from the influence of political forces, drug manufacturers; physician buy-in; the administrative burden associated with such a program; questions about integration with local PTC in terms of their traditional education and monitoring functions; and, most important, program funding. On the question of funding for Committee operation and the preparation of review materials, suggestions included drawing upon OHA/OCOTH infrastructure and administrative resources, drawing upon the expertise (clinical, pharmacoeconomic, etc.) of member hospitals, and asking pharmaceutical manufacturers to help prepare and support the cost of reviews.

Observations

- Ontario teaching hospital PTCs vary widely in size and composition.
- Few PTCs apply standardized methods for evaluating the quality of evidence supporting a product or seek input from individuals with formal training in economic evaluation. These gaps are reflected in pharmacy directors' varying levels of confidence in reviewers' abilities to find and properly consider relevant evidence.
- Few PTCs have formal, written policies for disclosing conflicts of interest.
- Hospital PTCs operate in institutions with different organizational structures and accounting systems, each with its own incentives and disincentives for and obstacles to managing drug utilization, containing costs, and sharing benefits.
- Some utilization management strategies that are deemed effective, such as Unit-based pharmacists and drug utilization reviews, are used less than pharmacy directors wish due to resource limitations and a perceived shortage of trained personnel.
- Few institutions are in a position to fully capitalize on demonstrated benefits of information technology in this area (e.g., physician order entry, drug utilization, etc).
- OCOTH pharmacy directors support exploring options for centralizing the review, approval, monitoring, and funding of select in-hospital drugs.

SECTION V: Summary and Recommendations

Ideally, effective formulary management optimally addresses the drug approval process, negotiating of drug prices, monitoring of drug utilization and clinical outcomes to revise drug policy, and mechanisms to optimise compliance with drug utilization criteria. Detailed published evaluations on all of these steps are scarce. The results of our environmental scan indicate that most hospitals both internationally and nationally operate largely independently of one another. Perhaps the most innovative approach to managing drug utilization and costs is the Queensland model, which utilizes a central drug evaluation committee. Although a formal evaluation assessing the clinical and economic implications of such a process is not available, the process has excellent face validity. Other regions of Australia are moving in this direction. Furthermore, the Winnipeg Regional Health Authority (WRHA) has also established a central PTC for several hospitals in their region. It is anticipated that this approach will not only avoid duplication and ensures even access, but it has the potential to minimize the influence of biases that are more likely to affect formulary decisions made at a hospital level.

Our self-administered survey to assess financial indicators of drug expenditures in hospitals was poorly completed. Regardless, there appears to be significant variability in drug utilization and costs between hospitals. The financial pressures facing the primary source of funding for the hospitals (i.e. the government) may be under greater financial pressure than the hospitals themselves given the recent shift in provision of health care services from the inpatient to the outpatient environment. Consequently, optimizing internal processes may be recommended prior to seeking additional funding from external sources. We also acknowledge, however, that the availability of extremely high cost yet beneficial therapies may pose significant financial strains on hospital resources. For these drugs in particular, a judicious approach to evaluating its value, establishing utilization criteria, and monitoring its utilization would indicate a conscientious approach to drug management and may provide grounds for additional funding if needed.

While we observed a significant level of variability in the composition and functioning of OCOTH PTCs, we believe all hospitals strive for the common goal of making value-based decisions. Maximizing efficiency in better attaining this common goal may be more productive than changing practices at the individual hospital level. As other regions have done, we recommend exploring the possibility of an independent central PTC to maximize efficiencies in decision-making. Such a committee would be composed of highly trained clinical and technical experts to assess the merits of medications from both clinical and economic perspectives and make recommendations for the conditions for utilization. Numerous guidelines exist for examining the cost-effectiveness of drug therapies. Appendix VIII outlines reviews of two drug therapies using pharmacoeconomic guidelines established by the DQTC in Ontario. The two drugs of interest were abciximab for use in coronary stenting and infliximab for the treatment of Crohn's disease perianal fistulae. Initial analyses of selected pharmacoeconomic evaluations following these guidelines reveal that while abciximab may be comparable to other commonly used therapies with respect to cost-effectiveness, infliximab may have a significantly less impressive cost-effectiveness profile for the stated indication.

If agreement for such a committee were reached, the proposed next steps would be to develop a model that would suit the needs of OCOTH hospitals. We recognize that it may be difficult to implement a central PTC for all drugs in all hospitals immediately, however we do believe that initially only new and extremely expensive drugs may warrant consideration by such an expert committee. The conclusions

of this committee should be viewed as non-binding to all hospitals and would present a united front, backed by a sound and explicit approach to evaluating value, for soliciting funding for extremely high cost medications if necessary. Eventually, this central PTC could take on a more direct, active, and involved role in maximizing drug utilization efficiency. With the potential gains in efficiency realized from a more central process, resources at the hospital level could potentially be relieved to pursue more productive tasks. In sustaining the current health care system, we are now relying on collective efforts to maximize efficiencies more than ever.

REFERENCES

[1] Russell LB. The diffusion of new hospital technologies in the United States. Int J Health Serv 1976; 6(4): 557-580.

[2] Institute of Medicine. Assessing medical technologies. 1985. Washington, DC, National Academy Press.

[3] Willison D, Wiktorowicz M, Grootendorst P, O'Brien B, Levine M., Deber R et al. International Experience with Pharmaceutical Policy: Common Challenges and Lessons for Canada. CHEPA 2001.

[4] Jacobzone S. Pharmaceutical Policies in OECD countries: Reconciling Social and Industrial goals. 40. 2000. OECD. http://www.olis.oecd.org/OLIS/2000DOC.NSF/LINKTO/DEELSA-ELSA-WD (2000) 1

[5] CIHI. Spending on Drugs Outpaces Other Health Care Spending, Reports CIHI. http://www.cihi.ca/medrls/14mar2001.shtml. 3-14-2001.

[6] Health Canada. Drug Costs In Canada. 1997.

[7] Menon D. Pharmaceutical cost control in Canada: does it work? Health Aff (Millwood) 2001; 20(3): 92-103.

[8] Anis AH. Pharmaceutical policies in Canada: another example of federal- provincial discord. CMAJ 2000; 162(4): 523-526.

[9] KPMG. Review of the Therapeutic Products Programme Cost Recovery Initiative. 2000.

[10] Health Canada. Pharmaceutical Issues Committee Report: Drug Utilization in Canada. 9-16-1999. http://www.hc-sc.gc.ca/english/archives/releases/1999/99picebk4.htm

[11] CIHI. Core Indicators for the Prescription Drug Utilization Reports--Working Document. 2001. http://www.cihi.ca/Roadmap/Prescript_Drug/pdf/Core_Indicators.pdf

[12] PIC. Pharmaceutical Issues Committee Report: Drug Prices and Cost Drivers 1990-1997. Health Canada. 9-16-1999. http://www.hc-sc.gc.ca/english/media/releases/1999/99picebk3.htm#copy

[13] Gregoire JP. Inter-Provincial Variation in Government Drug Formularies. Can J Pub Health 2001; 92(4): 307-311.

[14] McMillan S. Chair, Task Force on High Cost Drugs. 1998. http://formulary.drugplan.health.gov.sk.ca/publications/taskforce%20on%20high%20cost%20drugs.pdf

[15] Anis AH, Guh D, Wang X. A dog's breakfast: prescription drug coverage varies widely across Canada. Med Care 2001; 39(4): 315-326.

[16] Bacovsky R. Provincial Drug Submission, Review & Approval Process; The Bacovsky Report. 1998.

[17] Jardine L. Pharmacist, NBPDP. 2001.

[18] Ontario Ministry of Health and Long-term Care. Ontario Guidelines for Drug Submission and Evaluation. September 2000. http://www.gov.on.ca/health/english/pub/drugs/drugpro/dsguide_mn.html.

[19] Ontario Ministry of Health and Long-term Care. Ontario Guidelines for Economic Analysis of Pharmaceutical Products. 2001. http://www.gov.on.ca/health/english/pub/drugs/drugpro/econ_toc.html.

[20] Laupacis A. Inclusion and exclusion of drugs from provincial drug benefit plans. Are we making the right decisions and who makes them? CMAJ 2002; 166(1): 44-47.

[21] Fassbender K, Pickard A. A Policy Impact Analysis of Pharmaceutical Cost Containment Strategies in Alberta. Working paper 00-12. 2000.

[22] Nakagawa B. Simon Fraser Health Region. 2001.

[23] Roberts N. Southeast Health Care Corporation. 2001.

[24] Mack SD, Demsey JW. Drug utilization: a regional approach. Leadersh Health Serv 1995; 4(1): 34-37.

[25] D'Sa MM, Hill DS, Stratton TP. Diffusion of innovation I: Formulary acceptance rates of new drugs in teaching and non-teaching British Columbia hospitals--a hospital pharmacy perspective. Can J Hosp Pharm 1994; 47(6): 254-260.

[26] D'Sa MM, Hill DS, Stratton TP. Diffusion of innovation II: Formulary acceptance rates of new drugs in teaching and non-teaching British Columbia hospitals--a drug development perspective. Can J Hosp Pharm 1995; 48(1): 7-15.

[27] Rogers EM. Diffusion of Innovations. 4th Ed ed. New York: Free Press, 1995.

[28] Jackevicius C. DUE: Pharmacy Specialty Group; UHN/Mt.Sinai. 2001.

[29] Hall KW. Winnipeg Regional Health Authority. 2001.

[30] Petrie A. Queensland PAS. 2001.

[31] Commonwealth Government of Australia. Pharmaceutical Benefits Scheme. Commonwealth Government of Australia. 2001. www.health.gov.au/pbs

[32] Queensland Health. Queensland Health: Annual Report 1999-2000. 2000. www.health.qld.gov.au

[33] Queensland Health. Standard Drug List for Queensland Public Hospitals 2000 (version 7). 2001. www.health.qld.gov.au/HealthLiving/Pharmaceuticals_HP.htm

REFERENCES

[34] Queensland Health. High Cost/Highly Specialized Drugs Program (HSD) (version 20). 2001. www.health.qld.gov.au/HealthyLiving/Pharmaceuticals_HP.htm

[35] WRHA. Winnipeg Regional Health Authority Website. http://www.wrha.mb.ca/healthin/index.shtml . 2001.

[36] Hall KW. One Health Region's Timid Steps to Confront the Sacred Formulary Cow. Can J Hosp Pharm 2000; 53(4).

[37] CIHI. Drug Expenditures in Canada 1985-2000. 2001. www.cihi.ca

[38] CIHI. Canadian Institute for Health Information. Hospital Report 2001: Acute Care. 2001. Ottawa: Canadian Institute for Health Information.

[39] M.Mackinnon. Drug Programs Branch, Ministry of Health and Long Term Care. 2001.

[40] Government Ontario. Cancer Care Ontario. New Drug Funding Program. CCO. 2001. http://www.cancercare.on.ca/treatment/newdrugs.html.

[41] Pater JL, Browman GP, Brouwers MC, Nefsky MF, Evans WK, Cowan DH. Funding new cancer drugs in Ontario: closing the loop in the practice guidelines development cycle. J Clin Oncol 2001; 19(14): 3392-3396.

[42] M.Nefsky. Cancer Care Ontario. 2001.

[43] Jonsson B. Economics of drug treatment: for which patients is it cost-effective to lower cholesterol? Lancet 2001; 358(9289): 1251-1256.

[44] Glennie JL, Woloschuk DM, Hall KW. High technology drugs for cancer: the decision process for adding to a formulary. Pharmacoeconomics 1993; 4(6): 405-413.

[45] Hill SR, Mitchell AS, Henry DA. Problems with the interpretation of pharmacoeconomic analyses: a review of submissions to the Australian Pharmaceutical Benefits Scheme. JAMA 2000; 283(16): 2116-2121.

[46] Langley PC. Meeting the information needs of drug purchasers: the evolution of formulary submission guidelines. Clin Ther 1999; 21(4): 768-787.

[47] Industry Commission. The Pharmaceutical Industry. 51. 1996. Canberra, Australian Government Publishing Service.

[48] Jacobs P, Bachynsky J, Baladi JF. A comparative review of pharmacoeconomic guidelines. Pharmacoeconomics 1995; 8(3): 182-189.

[49] Government of Australia. Interim Document to accompany the Guidelines for the Pharmaceutical Industry on Preparation of Submissions to the Pharmaceutical Benefits Advisory Committee: including major submissions involving economic analyses. Commonwealth Department of Health and Aged Care. 2001.

REFERENCES

[50] Allinson Y. Funding of pharmaceuticals in public hospitals: PBS under the probe. Healthcover 2001; 11(2).

[51] Kaye K. NSWTAG executive director. 2001.

[52] QHDAC. Queensland Health Drug Advisory Committee (QHDAC). http://www.health.qld.gov.au/HealthyLiving/Pharmaceuticals_HP.htm . 2001.

[53] Robertson MB, Dartnell JGA, Korman TM. Vancomycin and Teicoplanin Use in Victorian Hospitals. MJA 1999; 171:127-131.

[54] Victorian Drug Usage Advisory Committee (VDUAC). http://www.vduac.org.au/. 2001.

[55] Weekes LM, Brooks C, Day RO. Indicators for drug and therapeutics committees. Br J Clin Pharmacol 1998; 45(4): 393-398.

[56] Plumridge R. Western Australia. 2001.

[57] Weekes LM, Brooks C. Drug and Therapeutics Committees in Australia: expected and actual performance. Br J Clin Pharmacol 1996; 42(5): 551-557.

[58] NSW Therapeutic Assessment Group Drug Utilization Evaluation Support Group. Drug Usage Evaluation: A Selection of Practice Options. NSWTAG 1999.

[59] Bochner F, Martin ED, Burgess NG, Somogyi AA, Misan GM. How can hospitals ration drugs? Drug rationing in a teaching hospital: a method to assign priorities. Drug Committee of the Royal Adelaide Hospital. BMJ 1994; 308(6933): 901-905.

[60] McLean AJ, Ioannides-Demos LL, Tong N, Topliss D. Drug rationing in a teaching hospital. BMJ 1994; 309(6946): 54.

[61] PHARMAC. A Prescription for Pharmacoeconomic Analysis. 1999. www.pharmac.govt.nz/

[62] Pillans PI, Conry I, Gie BE. Drug cost containment at a large teaching hospital. Pharmacoeconomics 1992; 1(5): 377-382.

[63] Dillon A, Gibbs TG, Riley T, Sheldon TA. The National Institute for Clinical Excellence and Coverage of Relenza by the NHS. 2001. Informing Judgment: Case Studies of Health Policy and Research in Six Countries. http://www.milbank.org/2001cochrane/010903cochrane.html

[64] Rawlins M. In pursuit of quality: the National Institute for Clinical Excellence. Lancet 1999; 353(9158): 1079-1082.

[65] NICE. Guide to the Technology Appraisal Process. NICE 2001.

[66] Maynard A, Bloor K. Regulating the pharmaceutical industry. BMJ 1997; 315(7102): 200-201.

[67] PhRMA. Pharmaceutical Industry Profile. 2001. www.phrma.org/publications/publications/profile01/chapter7.phtml

REFERENCES

[68] RCP. The prescribing of costly medicines. RCP 2001.

[69] Garvey G, Jappy B, Stewart D, Williams A, Duffus PR, Maitland JM et al. Grampian Health Board's joint drug formulary. BMJ 1990; 301(6756): 851-852.

[70] Pacey S, Li Wan PA. A review of methods of drug cost management in hospitals. J Clin Pharm Ther 1998; 23(3): 171-177.

[71] Gould IM, Jappy B. Trends in hospital antimicrobial prescribing after 9 years of stewardship. J Antimicrob Chemother 2000; 45(6): 913-917.

[72] Danish Ministry of Health FAaF. The Microbial Threat (The Copenhagen Recommendations). 1-4. 1998. http://www.sum.dk/publika/micro98/index.htm

[73] Feely J, Chan R, Cocoman L, Mulpeter K, O'Connor P. Hospital formularies: need for continuous intervention. BMJ 1990; 300(6716): 28-30.

[74] Read C. Put pharmacists in the front seat. Health care Management 1993; 1:32-34.

[75] Karr A, Shulman R, Drayan S. Promoting a Drug Formulary. Pharmaceutical Journal 1996; 256:657-659.

[76] Cotter SM, McKee M. Models of hospital drug policy in the UK. J Health Serv Res Policy 1997; 2(3): 144-153.

[77] Fijn R, Brouwers JR, Knaap RJ, De Jong-Van Den Berg LT. Drug and Therapeutics (D & T) committees in Dutch hospitals: a nation-wide survey of structure, activities, and drug selection procedures. Br J Clin Pharmacol 1999; 48(2): 239-246.

[78] Merlis M. Explaining the Growth in Prescription Drug Spending: A Review of Recent Studies. 2000.

[79] Grabowski H, Mullins CD. Pharmacy benefit management, cost-effectiveness analysis and drug formulary decisions. Soc Sci Med 1997; 45(4): 535-544.

[80] ASHP. ASHP statement on the pharmacy and therapeutics committee. Am J Hosp Pharm 1992; 49(8): 2008-2009.

[81] US Pharmacopeia. Principles of a Sound Drug Formulary System. 2000. US Pharmacopeia. http://www.usp.org/

[82] Udvarhelyi IS, Colditz GA, Rai A, Epstein AM. Cost-effectiveness and cost-benefit analyses in the medical literature. Are the methods being used correctly? Ann Intern Med 1992; 116(3): 238-244.

[83] Campbell G, Sprague K. The state of drug decision-making: Report on a survey of PTC structure and practices. Formulary 2001; 36:644-655.

REFERENCES

[84] Mannebach MA, Ascione FJ, Gaither CA, Bagozzi RP, Cohen IA, Ryan ML. Activities, functions, and structure of pharmacy and therapeutics committees in large teaching hospitals. Am J Health Syst Pharm 1999; 56(7): 622-628.

[85] Motheral B, Grizzle A, Armstrong E, Cox E, Fairman K. Role of pharmacoeconomics on drug benefit decision-making: Results of a survey. Formulary 2000; 35:412-421.

[86] VA Formulary Analysis Committee IoM. Description and Analysis of the VA National Formulary. Blumenthal D, Herdman R, editors. 2000. National Academy Press, Washington, DC. www.vapbm.org/PBM/natform1.htm

[87] Nishimura LY, Shane R. Therapeutic dilemmas. An approach to the management of expensive pharmaceutical advances. Pharmacoeconomics 1994; 6(6):498-505.

[88] Jaramilla JP, Colombo J, Simon L. What strategies can be tried to keep costs of antibiotics and other high-priced drugs from becoming true budget busters? Hosp Formul 1994; 29(4):305-308.

[89] Seltzer JL, Wordell CJ, Nash D, Johnson NE, Gottlieb JE. P & T Committee response to evolving technologies: preparing for the launch of high-tech, high-cost products. Roundtable discussion. Hosp Formul 1992; 27(4):379-392.

[90] Ziegler EJ, Fisher CJ, Jr., Sprung CL, Straube RC, Sadoff JC, Foulke GE et al. Treatment of gram-negative bacteremia and septic shock with HA-1A human monoclonal antibody against endotoxin. A randomized, double-blind, placebo-controlled trial. The HA-1A Sepsis Study Group 5. N Engl J Med 1991; 324(7):429-436.

[91] Govmt Canada. Health Insurance Act - REGULATION 552 (Amended to O.Reg. 322/01) - GENERAL. 2001. http://www.e-laws.gov.on.ca/tocStatutes_E.asp?lang=en.

[92] Govmt Canada. Health Insurance Act - Chapter H.6. Health Insurance Act - Chapter H.6 (Amended by: 1992, c. 32, s. 15; 1993, c. 2, s. 12; 1993, c. 10, s. 53; 1993, c. 32, s. 2; 1994, c. 17, ss. 68-74; 1996, c. 1, Sched. H, ss. 1-35 ; 1996, c. 21, s.51; 1997, c. 16, s. 7; 1998, c. 18, Sched. G, s. 54; 1999, c. 10, ss. 1, 2; 2000, c.26, Sched.H, s.1; 2000, c.42, Sched., ss.17-19; 2001, c.8, ss.32, 33.). As of June 29, 2001. 6-29-2001. http://www.e-laws.gov.on.ca/tocStatutes_E.asp?lang=en.

[93] Govmt Canada. Public Hospitals Act - Chapter P.40 (Amended by: 1996, c. 1, Sched. F, ss. 3-15; 1997, c. 15, s. 16; 1998, c.18, Sched. G, s.70; 1999, c.10, s.5.). 3-22-2000. http://www.e-laws.gov.on.ca/tocStatutes_E.asp?lang=en.

[94] Govmt Canada. Public Hospitals Act - REGULATION 964 (Amended to O. Reg. 321/01) - CLASSIFICATION OF HOSPITALS. 2001. http://www.e-laws.gov.on.ca/tocStatutes_E.asp?lang=en.

[95] Govmt Canada. Public Hospitals Act - REGULATION 965 (Amended to O. Reg. 538/99) - HOSPITAL MANAGEMENT. 2001. http://www.e-laws.gov.on.ca/tocStatutes_E.asp?lang=en.

REFERENCES

[96] Davis DA, Thomson MA, Oxman AD, Haynes RB. Changing physician performance. A systematic review of the effect of continuing medical education strategies. JAMA 1995; 274(9):700-705.

[97] Thomson O'Brien MA OADDHRFNHEL. Outreach visits to improve health professional practice and health care outcomes (Cochrane Review). The Cochrane Library, Issue 4, 2001. 2001. Oxford: Update Software.

[98] Thomson O'Brien MA OADDHRFNHEL. Audit and feedback: effects on professional practice and health care outcomes (Cochrane Review). The Cochrane Library, Issue 4, 2001. 2001. Oxford: Update Software.

[99] Hunt DL, Haynes RB, Hanna SE, Smith K. Effects of computer-based clinical decision support systems on physician performance and patient outcomes: a systematic review. JAMA 1998; 280(15):1339-1346.

[100] Bates DW, Leape LL, Cullen DJ, Laird N, Petersen LA, Teich JM et al. Effect of computerized physician order entry and a team intervention on prevention of serious medication errors. JAMA 1998; 280(15):1311-1316.

[101] Folli HL, Poole RL, Benitz WE, Russo JC. Medication error prevention by clinical pharmacists in two children's hospitals. Pediatrics 1987; 79(5):718-722.

[102] Kilroy RA, Iafrate RP. Provision of pharmaceutical care in the intensive care unit. Crit Care Nurs Clin North Am 1993; 5(2):221-225.

[103] Leape LL, Cullen DJ, Clapp MD, Burdick E, Demonaco HJ, Erickson JI et al. Pharmacist participation on physician rounds and adverse drug events in the intensive care unit. JAMA 1999; 282(3):267-270.

[104] Baldinger SL, Chow MS, Gannon RH, Kelly ET, III. Cost savings from having a clinical pharmacist work part-time in a medical intensive care unit. Am J Health Syst Pharm 1997; 54(24):2811-2814.

[105] Herfindal ET, Bernstein LR, Kishi DT. Effect of clinical pharmacy services on prescribing on an orthopedic unit. Am J Hosp Pharm 1983; 40(11):1945-1951.

[106] Herfindal ET, Bernstein LR, Kishi DT. Impact of clinical pharmacy services on prescribing on a cardiothoracic/vascular surgical unit. Drug Intell Clin Pharm 1985; 19(6):440-444.

[107] Gattis WA, Hasselblad V, Whellan DJ, O'Connor CM. Reduction in heart failure events by the addition of a clinical pharmacist to the heart failure management team: results of the Pharmacist in Heart Failure Assessment Recommendation and Monitoring (PHARM) Study. Arch Intern Med 1999; 159(16):1939-1945.

[108] Bogden PE, Abbott RD, Williamson P, Onopa JK, Koontz LM. Comparing standard care with a physician and pharmacist team approach for uncontrolled hypertension. J Gen Intern Med 1998; 13(11):740-745.

REFERENCES

[109] Bond CA, Raehl CL, Franke T. Clinical pharmacy services, pharmacist staffing, and drug costs in United States hospitals. Pharmacotherapy 1999; 19(12):1354-1362.

[110] Hux J, Paterson JM. Audit and feedback to improve prescribing. Report prepared for the Ontario Program for Optimal Prescribing. 2000.

[111] Arseneau KO, Cohn SM, Cominelli F, Connors AF, Jr. Cost-utility of initial medical management for Crohn's disease perianal fistulae. Gastroenterology 2001; 120(7):1640-1656.

[112] Topol EJ, Mark DB, Lincoff AM, Cohen E, Burton J, Kleiman N et al. Outcomes at 1 year and economic implications of platelet glycoprotein IIb/IIIa blockade in patients undergoing coronary stenting: results from a multicentre randomised trial. EPISTENT Investigators. Evaluation of Platelet IIb/IIIa Inhibitor for Stenting. Lancet 1999; 354(9195):2019-2024.

[113] Lincoff AM, Califf RM, Moliterno DJ, Ellis SG, Ducas J, Kramer JH et al. Complementary clinical benefits of coronary-artery stenting and blockade of platelet glycoprotein IIb/IIIa receptors. Evaluation of Platelet IIb/IIIa Inhibition in Stenting Investigators. N Engl J Med 1999; 341(5):319-327.

[114] Daniels N, Sabin J. The ethics of accountability in managed care reform. Health Aff (Millwood) 1998; 17(5):50-64.

APPENDICES

APPENDIX I. INTERNATIONAL

A. DETAILED INFORMATION

The following paragraphs will describe PTC structure and function, and methods of dealing with high cost drugs in countries having the most readily available literature: Australia, New Zealand, South Africa, the Netherlands, the United Kingdom, and the United States.

AUSTRALIA

National

Management for the universal health care system in Australia is shared between the federal government or Commonwealth and the state governments. Currently, about 1/3 of the population is also covered by private insurance which is used in both public and private hospitals.[3] With an annual expenditure of about Aus$3 Billion[45] the Australian Pharmaceutical Benefits Scheme (APBS) oversees a national formulary, drug pricing and purchasing, and subsidized outpatient medicines.

The Commonwealth establishes the National Health Policy, which supports the Quality Use of Medicines (QUM), a policy advocating that medicines be used judiciously, appropriately, safely and efficaciously. To support the PBS and review national drug policy issues, the Australian Pharmaceutical Advisory Council (APAC) representing a broad range of stakeholders, was established in 1991. (See PBS Organizational Chart, Figure 1 below.) The Pharmaceutical Benefits Advisory Committee (PBAC) has 12 members and makes formulary recommendations to the Minister of Health and Aged Care regarding drug comparisons and cost-effectiveness, and to the Pharmaceutical Benefits Pricing Authority (PBPA). An economic (ESC) and drug utilization subcommittee (DUSC) assist the PBAC. One year later, the Pharmaceutical Health and Rational Use of Medicines (PHARM) Committee was created to review and promote QUM policy specifically and consists of 12 members representing general practice, pharmacy, nursing, consumers, health education, the behavioural sciences and the drug industry. A national journal of drugs and therapeutics, the Australia Prescriber, was confirmed by a recent PHARM committee review to have a key role in encouraging QUM country-wide although consumer concerns were thought to require more attention. The Pharmaceutical Benefits Advisory Committee (PBAC), established in 1954, has 12 members and make formulary recommendations to the Minister of Health and Aged Care regarding drug comparisons and cost-effectiveness. An economic (ESC) and drug utilization subcommittee (DUSC) assist the PBAC with economic evaluations and evaluate national drug use patterns respectively. The PBAC also makes recommendations to the Pharmaceutical Benefits Pricing Authority (PBPA), created in 1988, which recommends initial prices for new drugs or changes in prices for current drugs. A reference based pricing (RBP) plan was implemented in 1997 to include ACEIs, CCBs, HMG-CoA reductase inhibitors and H2RAs. B-blockers and SSRIs were initially on the list but were later removed. Information on the effectiveness of this program was not available.

An independent company, the National Prescribing Service, was funded in the 1997-8 budget to evaluate and promote QUM using educational activities, practice visits, prescriber feedback, clinical audits and case studies with feedback. Almost ¾ of general practitioners are involved in NPS activities. Plans are to expand this to include 100% of gp's. As of yet, the Medicare Services Advisory Committee, established in 1998, which focuses on health technology assessment, has not included pharmaceuticals as part of its mandate, in contrast to the National Institute for Clinical Excellence (NICE) in the UK.

Pharmacoeconomic Guidelines

Langley states that "the Australian guidelines are not necessarily a model that other countries or health systems should try to emulate. In [his] opinion, as they stand, they represent an unsatisfactory attempt to lend a degree of scientific rigor to the traditional cost-effectiveness analysis."[46] In September, 1996 the Australian government Industry Commission issued its final report on the guidelines.[47] "The most criticized aspect of PBS listing was the application of cost effectiveness analysis to listing and pricing decisions...the present approach is regarded as too prescriptive and influential in price negotiations." Langley also notes that the 1995 Australian guidelines would likely be considered unreasonable in the United States, that they inflate the ability of costing information based on clinical trials to accurately predict costs in actual practice, and that they do not adequately account "for the indirect and intangible costs and benefits and wider health benefits of drugs".[46] Several Australian pharmaceutical manufacturers considered the drug submission process with its emphasis on cost-effectiveness as a means to delay introduction of drugs into the Australian market.

In fact, a report by Hill (of the Discipline of Clinical Pharmacology, Faculty of Medicine, University of Newcastle, New South Wales), Mitchell and Henry (a former chair of the ESC) published in 2000 in JAMA found significant problems of interpretation in the pharmacoeconomic analyses of over two-thirds of submissions to the APBS.[45] Hill commented that "the resources required to identify and correct these errors "may be beyond the capacity of many organizations, including peer-reviewed journals."

Jacobs et al from the Faculty of Pharmacy, University of Alberta compared 4 sets of pharmacoeconomic guidelines including those from Australia, Canada (CCOTA and Ontario) and the England and Wales Department of Health.[48] While noting frequent differences amongst these documents in areas including outcome selection, costs and perspectives, it is emphasized that "there is more than one 'right' way to conduct an economic efficiency analysis" and that "many cost-effectiveness measures are in the developmental stage." Table 2 in Appendix I summarizes the findings.

Drug Evaluation

At the national level, a document outlining the role and responsibilities of, and guidelines for drug submissions to the PBAC was first published in 1992, revised in 1995 and recently updated. [49]Created for the Australian pharmaceutical industry, these guidelines outline the details required for the proposed drug and its uses in the APBS, along with the necessary clinical and economic data, estimated use and financial impact. As the first pharmacoeconomic guidelines to be issued by a government authority, they have been described by Langley (Adjunct Professor, Department of Pharmaceutical Care and Health Systems, University of Minnesota College of Pharmacy; and US and International Manager, Health Economics with 3M Pharmaceuticals) as the "most comprehensive and widely referenced formulary submission guidelines" [46]. As such, Australia has in many ways been considered an international leader in drug evaluation and formulary management.

New drug submissions are made to the Department of Health and Aged Care (DHAC), which verifies the literature search, and trial results, and tests the assumptions. The Economic Subcommittee (ESC) of the Pharmaceutical Benefits Advisory Committee (PBAC), comprised of experts in health economics, decision analysis, clinical epidemiology and biostatistics, also examines the evidence. Their findings and

recommendations are presented to the parent PBAC which is composed of family practitioners, other specialists, clinical pharmacologists, pharmacists and a consumer representative. Subsequent recommendations are made to the health minister who makes the final decision. [45]

Possible Reforms

The Commonwealth has been considering major reforms to funding and delivery of services in the health care system, including making the funding of all medical services and pharmaceuticals, including those administered in public hospitals, a national responsibility. "A single funder is required for both inpatient and non-inpatient pharmaceuticals in public hospitals. The model must remove incentives for cost shifting between funders or within hospital budget cost centres." [50]

State

In-hospital medication and treatment are the responsibility of each of the six states. Public hospitals are responsible for all inpatient drug costs. Drug budgets comprise about 5-6% of hospital budgets and are therefore closely monitored. However, in some cases budgets are allocated to clinical units, while in others the drugs budget is administered 'centrally'. Hospitals in all states are required to have a Drug Committee, which, with the exception of those in Queensland, is responsible for deciding which drugs should be available. The issue of rapidly increasing drug costs is therefore a major issue for these hospital committees.[51]

Queensland

With a population of over 3 million, Queensland is the only state in Australia to have a central PTC which sets the state-wide formulary. Please see *Section II: Experience With Centralized Hospital Formularies.* The SDL is developed and maintained by the QHDAC. All drugs, both in- and out-patient, are purchased through a central pharmacy at prices negotiated by the Commonwealth Pharmaceutical Benefits Pricing Authority (PBPA), with plans for the 'profit' to be used to fund statewide programs such as Poisons and Drug Information Centres. Prescribing restrictions, such as limiting prescribing authority to certain specialists, are intended to control the availability of new drugs "until there is a satisfactory...experience gained with their efficacy and toxicity"; and to limit the "availability of expensive items to treat specific diseases which cannot be managed by other more economical and well established drugs."[52] Requests for additions to the SDL must come from prescribers (not drug reps) via hospital drug committees when possible. Evidence of efficacy and toxicity, comparisons with alternative drugs and estimates of hospital and state-wide cost-impact are requested.

Victorian Drug Usage Advisory Committee (VDUAC)

VDUAC is comprised of 9 representatives of key medical, pharmaceutical and health organizations. The Victorian Drug Usage Evaluation Group with 18 members currently was formed in 1996 "in recognition of the need to consolidate the statewide network of clinical pharmacologists, pharmacists and other clinicians involved in drug usage evaluation studies. The broad aim of the group is to facilitate and develop DUE activities in Victorian hospitals and to promote a coordinated approach which will optimize the value of such activities and achieve economies of effort.

The VDUAC provides active support for projects of mutual interest and facilitates dissemination of the information generated by the group to a wider audience. The VDUAC provides administrative services for the Victorian DUE Group. Recent studies have examined use of vancomycin and teicoplanin [53] and ceftriaxone and cefotaxime (report pending). The Victorian DUE Group in collaboration with the New South Wales Therapeutic Assessment Group (NSW TAG) and the Queensland DUE Group has been awarded funding from the National Prescribing Service (NPS) to carry out a multi-centre study of the antibiotic treatment of lower respiratory tract infection in emergency departments. The report is expected to be released in November 2001. [54]

New South Wales Therapeutic Assessment Group (NSW TAG)

The NSW TAG, modeled after the VDUAC, was founded in 1988 by pharmacists and clinical pharmacologists, representing 19 teaching hospitals, academic units and drug information services in NSW, and over 50 affiliate members from other Australian states, New Zealand and the South Pacific. Although TAG is a state funded organization, it is independent of government and industry, and makes non-binding drug policy recommendations to member hospitals. It also provides advice when requested to the State Government. Other (non-teaching hospitals) are supported via an electronic outreach program, called TAGNet. Additional functions include lobbying on behalf of member hospitals with government for such issues as funding for specific drugs or IT infrastructure to support QUM, with industry to deal with specific clinical issues. TAG also conducts regular audits of high cost drug use and multi-centre DUEs in member hospitals, and tracks therapeutic issues such as ADRs. In addition, NSWTAG prepared a template for drug submissions in 1997, and provides a number of policy and position statements for issues such as the contact between pharmaceutical reps and hospital staff, as well as for specific drug groups and classes.

In 1998, Weekes et al, representing NSW TAG, published a set of proposed PTC indicators field tested in 16 hospitals (Table 1, Appendix I) [55]. These proposed characteristics of an ideal PTC, provided standards by which to compare committees nationally and internationally. In an evaluation of TAGNet these indicators revealed a trend towards improvement in participating hospitals in comparison with uninvolved facilities (although not statistically significant since numbers were small - unpublished data).[51]

Western Australia

A state tender for public-sector hospitals covers about 60% of drugs, but hospitals purchase the remainder, which tend to be lower volume/lower cost drugs, independently. All hospitals in Perth undertake their own reviews of new medications, and thus there is much duplication of the review process. However, state funding may shortly become available to create a central committee charged with comprehensive evaluation of new high cost drugs.[56]

Institutions

Hospitals here as elsewhere in the world have undergone significant changes particularly in the last ten to fifteen years. This has included movement towards shorter length of stay, more ambulatory services, budget cuts, decentralized management and greater numbers of new and expensive medicines in a context

which has increasingly emphasized rational and cost-effective medical practice.[57] These changes are reflected in the increasing proportion of hospitals in Australia with a PTC which has risen from 70% in 1982 to 94% in 1995 [55]. A 1995 national survey[57] compared 306 committees representing teaching, urban non-teaching, regional, rural district, subacute and private hospitals. The average committee size was 9 but ranged from 3-23, and over 90% of these committees contained internists, pharmacists and nurses. Fewer than 50% had representation from surgery, primary care, finance, pharmacology or consumers, although teaching hospitals had significantly higher representation by pharmacologists and DUE pharmacists. Not surprisingly, high cost drugs were found to be a major concern. The information required in drug submissions most commonly concerned questions of therapeutic alternatives, efficacy, cost and estimated use.

Most PTCs (at least 2/3) were involved with drug use evaluations (DUE), medication errors and adverse drug reactions. The most common strategies to implement policies and manage the formulary were distributed guidelines, prescribing restrictions and monitoring by a clinical pharmacist. Educational and behavioural interventions including audit and feedback, drug bulletins and staff presentations were used in over 90% of the facilities. The committees however were looked upon with only moderate acceptance by hospital administration and medical staff. On the whole, cost-effectiveness data was found to be minimally available, as was access to DUE pharmacists, pharmacologists and c-e experts.

Primary expectations of PTCs included the adherence to the principles of best practice, equal access, transparency, consultation, ethics and education; and primary activities included attention to policy, rational use and cost containment, adverse event monitoring, formulary management and education. Much less commonly infection rates, antimicrobial resistance and readmission rates were considered. Self evaluation revealed that about three-quarters of the decisions were implemented, and that the PTCs in teaching hospitals were perceived to be more effective.

As a result of a survey conducted of 37 hospitals published in 1999, NSWTAG found that, as expected, DUEs were more commonly performed in larger centres.[58]. Funding for the DUE pharmacist was not reported for about 1/3 of the hospitals, but the pharmacy staff budget was the most common source at 20%.

Melbourne Teaching Hospitals' Drug Usage Group (MTHDUG)

MTHDUG, part of the VDUAC network, is a group comprising directors of pharmacy, clinical pharmacologists and other clinicians from major Melbourne and regional hospitals who meet regularly to exchange drug usage data and to discuss drug usage issues. Member hospitals contribute specific drug use policies which form a database of useful templates. With eleven hospitals or networks represented as full members of MTHDUG and a further seventeen associate members, the group also has a significant lobbying role, both at an institutional and government level.

Dealing with High Cost Inpatient Medications: Two Hospital Case Studies

"Most teaching hospitals are likely to be faced with the dilemma of shrinking resources. One solution is to obtain increased funding; another is to impose measures to enable targeting of available resources to activities that are considered to be the most cost effective. Since the first option is becoming increasingly

difficult to achieve, and in the view of some, to justify, this realistically leaves only the second option if teaching hospitals are to continue their traditional roles."[59] Bochner et al describes one approach taken by The Royal Adelaide Hospital, in South Australia, a 900-bed tertiary referral and teaching hospital. Faced with a fixed drug budget, the PTC developed a 'ranking model' to maximize objectivity and consistency of the decision process using a sound cost-effective evaluation and establishment of clear protocols and treatment guidelines. A combination of quality and cost scores were used to create a hierarchy for allocating resources. Although Bochner states that the ranking was successful, he does not report patient outcomes resulting from use of this method, nor is there any long term follow-up in the literature.

In response, McLean et al[60] suggested that drug budgets "can be contained by a process other than rationing by prioritization" and presented the experience at Alfred Hospital, Melbourne (Victoria). Despite a complex caseload and an increase in annual volume of about 11%, the drug budget had been contained to under about 5 1/2 %. Careful attention to prescribing patterns for over 10 years with aggressive DUR programs which have targeted not only high cost items but those "drug items that influence overall costs of care and outcomes" have underpinned their success. They also questioned the validity of an arbitrary ceiling on pharmaceutical costs, since an expensive new drug which could result in substantial savings elsewhere might well be justified.

NEW ZEALAND

This country has experienced significant health system reform in recent years. The national Health Funding Authority was created in 1998 as a result of the merging of 4 regional health authorities. PHARMAC (Pharmaceutical Management Agency) is responsible for national pharmaceutical policy. Primary care organizations have been contracted to manage pharmaceutical budgets. In the evaluation of new drugs, PHARMAC uses cost-utility analyses to guide resource allocation, discounting to obtain present values of future costs and benefits, and sensitivity analysis to determine to what extent the results depend on the assumptions made.[61]

SOUTH AFRICA

A 1500-bed teaching hospital reported results of its drug cost containment efforts in the early 1990's. [62] Faced with increasing drug prices but a reduced pharmaceutical budget, 15 major drug categories were reviewed by the Medicines Control Committee (MCC). Based on a detailed audit of the previous year's drug expenditures, with particular attention focused on expensive agents, therapeutic substitution, deletion of non-essential drugs from the formulary, prescribing restrictions and fixed budgets, 20% savings in the drug costs was realized the next year. 65 items were deleted from the formulary, and a decrease in spending was achieved in 14 of the 15 categories, the exception being lipid-lowering agents. Expensive agents were not defined and no patient outcomes were reported.

APPENDIX I. INTERNATIONAL: DETAILED INFORMATION

UNITED KINGDOM

National

The National Health System (NHS), established in 1948, provides universal health care coverage virtually free at the point of service and financed primarily from tax revenue. Some individuals are subject to flat-rate charges for prescriptions but most are exempt. Only about 11% of the population has some form of private insurance. Hospital staff--including physicians-- are salaried.

In the last decade or so, the United Kingdom has undergone a number of significant changes in an attempt to improve delivery of cost-effective care. In *'The Way Forward for Hospital Pharmaceutical Services'* published in 1988, the importance of PTC's role in helping to provide better patient care was acknowledged, calling for more cost-effective use of drugs and increased pharmacy support for the committees. The following year, the NHS white paper, *'Working for Patients'* set the stage for the creation of decentralized clinical directorates and corresponding drug budgets within hospitals. The Cochrane Collaboration Centre and the Department of Health's Health Outcomes Group were both established in 1992, and a major policy statement on *'Purchasing and Providing'* was released in 1994. Two years later *'Improving Clinical Effectiveness*', encouraged strategic guideline development and comparison of health care interventions with particular emphasis on drug therapies.

National Institute for Clinical Excellence (NICE)

NICE was created in 1999 as a result of three main forces: increasing pressure of costs, particularly pharmaceuticals; inconsistent health care rationing decisions, and the desire to improve the quality of care.[63] NICE's chairman Michael Rawlins indicated that the institute had been established "neither to cut costs, nor to introduce rationing, but to help the NHS get value for money."[64]

The NHS subsequently commissioned NICE to develop guidelines to aid in the assessment of certain technologies, including drugs, based on evidence of their social value and impact on health budgets. These guidelines, which are used in the NHS appraisal process, outline the information required in the clinical and economic assessments of these technologies and medicines. ([65] In October 1999, NICE ruled against the NHS in its use of zanamivir (Relenza) on the basis that the drug was of only moderate benefit in otherwise healthy individuals. The evaluation of this drug had been 'fast-tracked', taking 3 months instead of the usual 10-12. NICE's ruling prompted important questions to be raised regarding the "criteria for decision making, the role of costs, and the degree to which decisions of NICE and the secretary of state would be binding on clinicians."[63]

Pharmaceutical Price Regulation Scheme (PPRS)

The PPRS is responsible for the pricing of prescription drugs in the UK. This is a voluntary agreement between the Department of Health and the Association of the British Pharmaceutical Industry by which companies negotiate prices based on drug sales to the NHS. There is increasing pressure on the NHS to have comparative cost-effectiveness proven before new drugs and technologies are purchased. Currently, licensed drugs can be publicly prescribed unless they are removed, creating a negative list.

If a 'fourth hurdle' (after the 3 recognized phases of clinical trials representing criteria for marketing approval: safety, efficacy, and quality) for drug approval was formed by creating a cost-effectiveness requirement, this could do the following: create a positive national list of publicly reimbursed

medications, help in the prioritizing of drug treatments as well as possibly help reduce 'postal code prescribing' where access is variable across the country.[66] in [63] The pharmaceutical industry, on the other hand, reports that "a 'fourth hurdle' is widely agreed to be counterproductive for new drug development. The full therapeutic, social, and economic value of a product is often apparent only after it has been on the market for several years."[67]

'The Prescribing of Costly Medicines'

This Working Party Report prepared in 2000 [68],by the Royal College of Physicians addressed the need for establishing criteria for the use, monitoring and funding of costly medicines. Costly medicines were defined as "one that is expensive when the overall cost of its use is compared with the overall cost of using currently recommended treatment (which may or may not involve a medicine)". Recommendations included the following:

- advising the NHS not to agree to purchase costly medicines of unproven clinical effectiveness or cost-effectiveness, pending appropriate evaluation by NICE or additional research conducted in authentic clinical settings;
- ensuring transparency of priority-setting at all levels;
- central funding for all costly new medicines whose use will not be net saving via a separate guaranteed funding stream;
- establishing 'area prescribing committees' by local drug purchasers to review costly medicine recommendations and establish local guidelines;
- ensuring unavailability of any medicine not purchased by the NHS except by private prescription.

Regions

Joint hospital/community drug formularies such as that of the Grampian Health Board, have been created to help bridge the gap between primary and secondary care. ([69] in [70]. Gould et al [71] describes in- and out-patient antibiotic prescribing trends in all Grampian hospitals which have been monitored prospectively for 11 years since 1986. An antibiotic committee introduced a policy and formulary in 1989 but it has had only limited success in controlling prescribing. From 1992/3 to 1996/7, 22 new antibiotics were considered for inclusion in the hospital formulary of which 17, including 7 antiretroviral agents, were incorporated, all for restricted use only. Despite these restrictions, expenditure on antibiotics more than tripled since 1986/7 and increased 50% since 1992/3, two-thirds of the latter increase being due to the use of new drugs, particularly anti-HIV drugs, lipid amphotericin derivatives and teicoplanin (an antibiotic with a similar profile as vancomycin but reportedly with less toxicity). Besides encouraging professionals towards better prescribing practices, the author states that "there is a limit to what can be accomplished without dedicated resources for audit and multi-disciplinary antibiotic teams as recommended in the Copenhagen Declaration.[72] Audit will be easier when computerized prescribing is available, but this seems some years away."

Pacey states that the factors considered integral to a formulary's success include peer review, continuous prescriber feedback, educational and promotional programmes, continuous monitoring and an effective PTC, along with close collaboration between doctors and pharmacists. A study published in the BMJ in 1989 found that with the introduction of a formulary and active intervention, generic prescribing rose by 50%, inappropriate prescribing fell and compliance was good, with only those prescribing behaviours targeted by the intervention being affected.[73] in [70].

Institutions

PTCs increased in the UK from 52% in 1981 to 92% in 1987. [70]. Several observations were made regarding PTCs structures and functions. They were becoming increasingly multidisciplinary, exerting control over the formulary, involved in treatment guidelines and education, and using DUEs more frequently for cost containment and budget prediction. Drug submissions did not require pharmaco-economic assessments, although in 1994, the UK moved a step forward with the Association of British Pharmaceutical Industry, ABPI, and Department of Health document, 'Guidance on good practice in the conduct of economic evaluations of medicines'. These guidelines have been criticized because they involved minimum consultation those in the field, were based on inadequate evidence and that they presented little monitoring guidance.[70]

The clinical directorates described in the 1989 NHS white paper were typically composed of a clinical director, business manager, senior nurse and an accountant. The financial impact of creating the clinical directorate pharmacists has been reported to be substantial: as much as £90K in one year in one institution and £100K in another.[74] in [70]

Further methods to improve drug use have included group purchasing, improved stock control and waste reduction; therapeutic substitution, although this is a more recent phenomenon in the UK than the US; treatment guidelines; and drug cost information provided to physicians and clinic directors, with monthly prescribing cost feedback.

Formulary promotion also has been demonstrated to be important. The University College London Formulary has been promoted successfully using techniques common to marketing, including personal selling, advertising campaigns, sales promotion, publicity and external promotion.[75] in [70]

In another survey of 8 hospitals intended to be representative of UK NHS hospitals, Cotter et al [76] identified 3 models of drug policy. The traditional model, the most common, develops hospital-wide drug policy in a cooperative manner by multidisciplinary groups. Scientific, clinical and financial principles are used to encourage rational prescribing and to control costs. New drugs are typically permitted a trial period accompanied by literature review and cost-effectiveness evaluation. Initially, in this model formularies were thought to be a means to reduce expensive and inappropriate treatments; however formularies have revealed an increasing sense that many services are currently under funded.

Cotter's second model, the combined model, is described as a specialty-oriented variation on the traditional hospital-wide model. It is favoured at hospitals with specialist or directorate pharmacists, and were created to address the problem of insufficiently detailed information to support decision making. The major weakness of this model is that there is a trend towards a fragmented, disconnected formulary as opposed to a single hospital-wide formulary as in the traditional model.

The medical control model was present in only 1 of the 8 sites. There was no hospital-wide formulary or even a PTC in place because the philosophy was that specialists needed complete freedom to develop new therapies. However, this model appears to be a dying breed as it is confronted with the every-increasing pressure to adopt a formulary, audit drug use and allocate limited resources.

Neither the patient nor financial outcomes of any of these models are documented here.

THE NETHERLANDS

National

A hybrid public-private health care system is in place in this country, financed by social insurance contributions from employers and employees. The National Health Insurance Council is responsible for establishing most pharmaceutical policy such as price ceilings and positive lists. Attempts are being made to encourage Sickness Funds to work with pharmacists and physicians to more actively manage health benefits (such as establishing local formularies). About 2/3 of the population receive treatment in the public system. [3]

Institutional

D&T Committees

Dutch legislation introduced in 1984 required each hospital to convene a PTC including at least one pharmacist, physician and nurse, although in the Netherlands as in most European countries, DT committees date back to the 1970s. In 1986, 87% of all Dutch general hospitals had a PTC, and this has risen to about 98% over a decade later. These numbers are typical throughout much of the European Community.[77] Theoretically Dutch PTCs are not responsible for drug expenditures, but most hospital boards have informally passed on this responsibility to them.

A survey by Fijn et al in 1999[77] identified many of the structural and policy characteristics of Dutch hospitals. His inclusion criteria included facilities with over 300 beds, with a PTC possessing a written statute and a printed drug formulary, and he based his survey on the Australian Indicators developed by Weekes et al.[55] Fifty-four hospitals, including 7 teaching, met the criteria and his response rate was 70%. Over three-quarters of these institutions were responsible for only one facility, however the balance were responsible for up to 9 others such as nursing homes and psychiatric facilities. About 60% had up to 20 subcommittees, and the average PTC membership was 8 with a range between 3 and 14. The committee size is typical of some countries such as Ireland, but smaller than those in Germany which may have as many as 40 members. Besides pharmacists and internists who were almost universally present, other medical specialties were often represented in subcommittees. Clinical pharmacologists were found in about 1 in 4 PTCs. Only 7 of the 38 PTCs surveyed had economic, QA or administrative representation.

In comparing theoretical with actual responsibilities, general prescribing policies, hospital formulary control and maintenance, and assurance of cost-effective delivery of health care, were consistent. However the monitoring of prescribing patterns and policy compliance often fell considerably short of expectations. On the other hand, although in theory the General Board of Hospital Management (comparable to the Medical Advisory Committee) was responsible for drug expenses, this responsibility frequently unofficially was passed on to the PTCs. The Dutch Association of Hospital Pharmacists (ASHP) created a model statute in 1989 which stated that PTCs should oversee the HDF, play an

important role in cost-effective policy as well as in drug distribution, information, education and utilization evaluation. Dutch PTC tend not to be involved in educational or promotional activities.

All PTCs recognized drug company marketing strategies, and many acknowledged this influence in the quality of clinical data and in prescribing patterns. Regarding conflict of interest policies, 35% of the PTC's required absolute transparency, half required a declaration for only a few drug groups and 10% had no policy.

Drug submission and evaluation

This process is similar to that in other countries; original research, pharmacoeconomic guidelines and drug manufacturer information are considered. Many Dutch PTCs are not familiar with meta-analysis and prefer to react to physician's requests for formulary additions or changes rather than being proactive. 80% of PTCs consider pharmacists or pharmacotherapeutic experts to have the greatest influence formulary drug selection. About 3/4 of the committees primarily replaced drugs on the HDF with new ones, whereas most of the balance mainly added drugs. Of the 30 added to the Dutch market each year, an average of 15 drugs was added to the HDF annually. The specialties in which consensus was most difficult to achieve were cardiology, followed by internal medicine, psychiatry and anesthesia. And the drug groups which proved most complicated to evaluate were cardiovascular drugs, antiemetics, radiological contrast agents and antidepressants. It was suggested that in cardiology, internal medicine and psychiatry, individual experience and drug company marketing had a particularly strong impact on the opinions of these physicians. Psychiatrists were often reluctant to choose one drug over another because of pressure from patients and patient organizations and the belief that clinical outcomes for a drug often varied significantly in individual patients.[77]

USA

National

Outpatient Prescription Drugs

Review of outpatient prescription drug utilization and spending may provide a useful context to demonstrate some of the pharmaceutical issues common to both in- and out-patient settings.

In his 2000 report for the US Department of Health and Human Services, Merlis reviewed 4 studies, 2 from private industry and 2 from independent researchers. New brand-name drugs, some of which replace existing, less costly treatments and some of which help with untreatable conditions account for much of the increase in use and spending.[78] About 40% of the spending growth was for medications introduced after 1994. New drugs also were more expensive. The average drug cost in the last half of the 1990s was about two-and-one-half times that of existing drugs. About half the spending increase attributable to new drugs was due to utilization, about half to the fact that they cost more.

A few therapeutic categories were particularly problematic. These included:

- Cardiovascular, especially cholesterol reducers and antihypertensives
- Gastrointestinal, especially anti-ulcerants
- Psychotherapeutics, especially antidepressants
- Anti-infectives

- Hypoglycemics or anti-diabetics
- Antihistamines
- Asthma medications
- Pain relievers

The first five of these accounted for about half of all increased drug spending during the middle and late 1990s.

Forecasts of future drug spending growth show continuing annual increases in the range of about 10 to 20 percent over the next several years. New drugs now in the "pipeline"-awaiting FDA approval-may account for as much as 50 percent of spending growth in the next five years.[78]

Pharmacy Benefit Management (PBM)

In the last decade, PBM companies have become a major provider of outpatient services and medications. PBMs attempt to influence drug use, prescribing and costs by a variety of means including "generic substitution, formularies, preferred drug lists, therapeutic interchange programs, treatment guidelines, DURs, and prior authorization."[79] Use of cost-effectiveness studies in formulary decision was found to be limited by perceived problems with the comparison drug or therapy, the relevance of the patient population, methodology and objectivity of pharmaceutical industry studies. Resolving these weaknesses would also enhance the usefulness of cost-effectiveness studies in the hospital setting as well. Five PBMs surveyed indicated they would like to see the following enhancements to make cost-effectiveness information more useful:

- head-to-head comparisons among market leaders;
- studies performed on relevant populations;
- timely availability of information;
- independent sponsorship or no-strings funding;
- publication in leading peer-reviewed journals;
- more sophisticated drug reps able to discuss nuances of a study.

In-patient Prescription Drugs

D&T Committees

D&T Committees have existed in the US since the 1930s, but it was not until 1965 that the Joint Commission on Accreditation of Hospitals mandated the development of hospital formularies. An official description of the role of PTCs was created in 1959 as a joint effort of the American Society of Hospital Pharmacists (ASHP) and the American Hospital Association. The ASHP released a 1992 statement [80] which addressed the committee's purposes, organization and operation and functions and scope. Further to this, a document entitled [81] was endorsed by a coalition of national organizations including the ASHP, AMA and the USDVA.

Rules for cost-effectiveness analysis have been widely disseminated since the 1970s. But in 1992 Udvarhelyi et al demonstrated that these rules and the principles behind them were being largely ignored.[82] However due to the unprecedented pace of prescription drug spending, in the last decade

APPENDIX I. INTERNATIONAL: DETAILED INFORMATION

US health organizations and facilities, like their international counterparts, have been forced to try to contain costs without comprising health care quality.

National Surveys

(summarized in Table 2, Appendix I)

Some of the consequences in the struggle for cost-effective drug use, are reflected by Campbell and Sprague in their recent survey of PTCs include widespread adoption of tiered copay benefits, increased use of pharmacoeconomic methods for drug evaluation as well as prior authorization requirements and therapeutic interchange.[83] Adding to the pressure is the explosive increase in direct-to-consumer advertising along with the record number of new drugs introduced in the late 1990s.

This 2001 national survey of about 1000 subscribers to 'Formulary' virtually all of whom either were or had been on PTCs, or who were contributors. 70% of them represented independent hospitals or health systems, 10%, Managed Care Organizations (MCO), about 10%, Long-Term Care or Pharmacy Providers and about 5%, government agencies. The complete findings are summarized in Table 7 (Appendix I). Notably, pharmacoeconomists or outcomes analysts were present in fewer than 1 in 5 PTCs. Along with information technology specialists and patient privacy officers, these latter two positions were anticipated to be the most likely additions to PTCs in the next 2 years.

Furthermore, drug evaluation was more commonly initiated prior to FDA approval if the drug was expected to be a 'budget-buster', and more likely to be delayed if it was a 'me-too' drug or a new indication or formulation of an existing drug. The Academy of Managed Care Pharmacy (AMCP) released a format for formulary submissions in 2000, however the degree of preparation and time, along with the pharmacoeconomic and technological expertise required were thought to be significant barriers to implementation. Less than 15% of those surveyed indicated their facility was considering using the AMCP template.

Government facilities were more likely to emphasize drug costs and coordinate with other organizations in decision-making, conduct DUEs, and develop programs to improve compliance including prescriber profiling. It was widely anticipated that in the next few years PTCs would become more influential and face increased scrutiny.

Three-quarters of the PTCs met at least on a quarterly basis, with 13 as the average number of members. About half of the PTCs had subcommittees and most of the rest had five or less. ID or antibiotic subcommittees were by far the most common (70% of PTCs with subcommittees), followed by cardiovascular (30%), guidelines or critical paths (25%) and drug errors/ADR subcommittees in about 25%. Less common were hematology/oncology, primary care, pediatrics, gi or drug contract subcommittees. Utilization review or QA officers were found in the majority of PTCs.

More than 70% of the PTC were involved in the following: reporting or monitoring ADR or medication errors; formulary inclusions or reimbursement decisions; development and review of guidelines and protocols; drug use policy and procedures; and conducting or approving DUEs. Other major activities included drug use staff education, evaluation of short-term medical savings for drugs under formulary review, development and review of disease management programs, and involvement in formulary appeals.

APPENDIX I. INTERNATIONAL: DETAILED INFORMATION

The major factors in evaluating new drug submissions, after safety and efficacy, the respondents reported that the potential for ADR or drug interactions, the impact on QOL and on total treatment costs, the acquisition price, the impact on LOS (length of stay) and patient restrictions were the most important considerations. About half of the PTCs would compare the new drug to the one it would replace; 40% would review the entire drug class (this was the more common approach in LTC facilities.); less than 10% would evaluate the drug on its own merits independently. 'Me too' drugs typically were added only if they were of comparable efficacy but less expensive. Weighing nonpharmacy savings or costs was common, and acquisition cost was more likely to be the major factor in 'preferred-nonpreferred' decisions as opposed to formulary inclusion decisions. Such decisions were often coordinated with other organizations and less frequently with national medical guidelines.

Those on the committee felt to have the strongest influence on decision-making were the pharmacy/formulary director, staff physician, medical director, clinical pharmacy specialist, drug information officer and staff pharmacist. Of note is that nurses, pharmacoeconomists and CEOs had only some or very little influence. External to the committee, pharmacists then mds were reported to have the most influence. The primary triggers of formulary changes included the availability of a generic equivalent or the addition of a cheaper drug with equivalent efficacy. And substantial physician prescribing was reported to be a major determinant only sometimes in having the new drug added to the formulary. This was even less likely in the managed care setting.

Large US teaching hospitals were the focus of a comprehensive 1995 survey by Mannebach et al.[84] This survey, described the PTC composition and activities. With respect to the drug submission process, pharmacists were nearly always primarily responsible for writing the formulary review. Over half the PTCs reported performing either a formal economic cost analysis or cost impact evaluation most or all of the time. However "it was not clear whether [PTC] decisions were based on economic, safety, efficacy or other factors." Evaluation of the PTCs effectiveness was also not included but it was noted that a useful standard for assessing this was lacking.

PTC membership averaged 19, with about 90% of those with the power to vote. Two-thirds of that number were typically physicians, about 3 were pharmacists, 2, nurses and 1, from administration. With respect to policy issues, almost ¾ of the committees had therapeutic interchange policies, and ½ had formal conflict of interest policies. In fact only 15% had a policy prohibiting drug representatives from contacting PTC members. The major activities of these PTCs included formulary control, DUE and the review of drug use policies and procedures. On average 18 new drugs were added to the hospital formulary in the previous year, and 16 were deleted. 90% of the HDFs were closed. Comparing the formularies using 3 drug groups, the authors found that the HDFs had an average of 2 H2RAs, 2 statins and 3 ACE inhibitors. All 4 H2RAs were present with nearly equal frequency on the HDFs, lovastatin was present on about 4 of 5, and captopril and enalapril plus one additional ACEI were most commonly found.

The information considered in these economic analyses always involved drug acquisition costs, alternate therapy cost analysis (70%), direct medical costs (55%) and indirect costs, resource impact and nonmedical costs in a substantial minority of instances. Formulary monitoring or DUE was not included in the survey, however decisions were most frequently communicated to medical staff by newsletter, although this has been demonstrated to be of little help in changing prescribing patterns.

In early 2000 another institution-level survey was conducted[85]. The focus here was on the role of pharmacoeconomics in drug benefit decision-making, and was completed by over 400 physicians and pharmacists from an MCO which represented only a 14% response rate. Pharmacoeconomic studies that demonstrated short-term medical savings and those showing higher cost and/or better outcomes were rated the most relevant, although, interestingly, two-thirds of the respondents indicated that pharmacoeconomic information only occasionally actually affected decisions. After safety and efficacy, the survey found that in the course of drug evaluations cost, followed by pharmacoeconomic considerations and physician demand were the most important factors. Cost-effectiveness and cost benefit analysis were identified as being most familiar and valuable to those surveyed—cost-utility and cost-consequency analysis proved to be least familiar. Regarding the major approach taken to pharmacoeconomic analysis, most were more familiar with clinical studies, less with claims data and least with decision-analytic models. Of note as well, about 40% of the respondents reported that pharmacoeconomic studies were performed in-house.

Veteran's Affairs (VA)

The Department of Veteran's Affairs National Formulary was implemented in 1997. Over twenty regional and local formularies are included in this National Formulary although some differences between them do exist. Between FY 1998 and FY 1999 VHA drug costs rose by nearly 20%. However, a report prepared by the Institute of Medicine in 2000 found that "savings in pharmacy expenditures approaching $100 million over the approximately 2-year time span since formulary implementation have probably been realized."[86] The closed and other classes with national committed-use contracts comprise about 15% of the projected $2 billion in VHA drug expenditures in FY 2000, an annual expenditure of $300 million or more. In return for volume commitments on selected medications, drug companies have reduced prices from 16-41%. Besides these cost saving measures, the VA uses blanket purchase agreements, generic contracts and bulk purchases.

Although patient outcome data was scarce, the IOM committee also found that there had been no increase in hospitalizations for illnesses treated by two of the closed drug classes, and that the formulary was not overly restrictive.

The lack of clear evidence to allow assessment of how utilization changes affect quality was also noted to be a common problem in the private sector as well. Further, the report determined that the National Formulary was not overly restrictive, and that, although it was a crude measure at best, veteran complaints about access to drugs was relatively infrequent. It did however recommend abandonment of the mandatory one year waiting period after FDA approval before accepting new drugs onto the formulary. This blanket policy was felt to be redundant to the FDA approval process which had already determined the safety and efficacy of new drugs, and inappropriate in the case of demonstrated significant new drug therapies.

Institutions: Dealing with High-cost Agents

Cedars-Sinai, a 1100-bed tertiary care teaching institution in Los Angeles, conducted a strategic planning process in the early 1990s to "address the effect of biotechnology on patient care and fiscal resources."[87] Two task forces comprised of relevant clinical specialists were established in 1991 to

oversee prescribing of colony-stimulating factors (CSFs) and anti-endotoxin monoclonal antibodies. Drug use criteria was developed based on a literature review and individual physicians on each task force acted as gatekeepers. Pharmacists screened the requests using the established criteria and any unclear cases were forwarded to the physician reviewer. Because of legal concerns and questions about physician autonomy, the orders of prescribing physicians who disagreed with the gatekeeper were carried out but were subject to follow-up by the respective peer review committee. 15% of the requests for CSF did not meet the usage criteria, and two years after the introduction of the guidelines, the actual CSF acquisition costs per admission in HIV-infected patients dropped by 60% ($US443). The number of doses per admission in the same patient group was also halved. Although not formally evaluated, the authors reported, based on discussions with the medical staff, that this approach did not result in any adverse outcomes. This lack of formal assessment of outcome is a significant weakness, but the study does illustrate one approach to dealing with high cost medicines while preserving physician autonomy.

Another teaching hospital's approach to prevent "high-cost drugs from becoming true budget busters" was described by Jaramilla et al[88] Between FY 1992 and 1993, Saint Joseph Hospital & Health Care Center, a 500-bed facility, experienced a rise of about 20% in drug expenditures. The PTC developed recommendations based on cost-effective alternatives. These recommendations were published alongside projected cost savings in the monthly PTC bulletin and presented in lectures to the professional staff. No long term follow-up was reported, but significant savings were seen after only 2 months.

The PTC at Thomas Jefferson University Teaching Hospital established a Technology Assessment Committee to deal with the rapid emergence of potentially revolutionary and costly biotechnological therapies. [89] In anticipation of FDA approval for the human monoclonal antibody, Nebacumab-for treating gram negative sepsis--the committee recognized the importance of proactive policy development. This drug which could be seen by many as a 'magic bullet', therefore had significant potential for expensive misuse and overuse, so guidelines were necessary to ensure it was used appropriately and to enable appropriate post-marketing evaluations to be conducted. The guidelines established were similar to those developed by Ziegler et al[90] and were a joint effort with the Technology Advancement Center of the University Hospital Consortium (UHC), an alliance of 56 US academic medical centers. A form, completed with the awareness of the attending physician, was required and approval granted by a representative from a consulting group comprised of infectious disease, pulmonary, anesthesia and critical care specialists. Since the window for administration was 12-24 hours adequate time was felt to be available for consultation. Legal and ethical considerations also were taken into account.

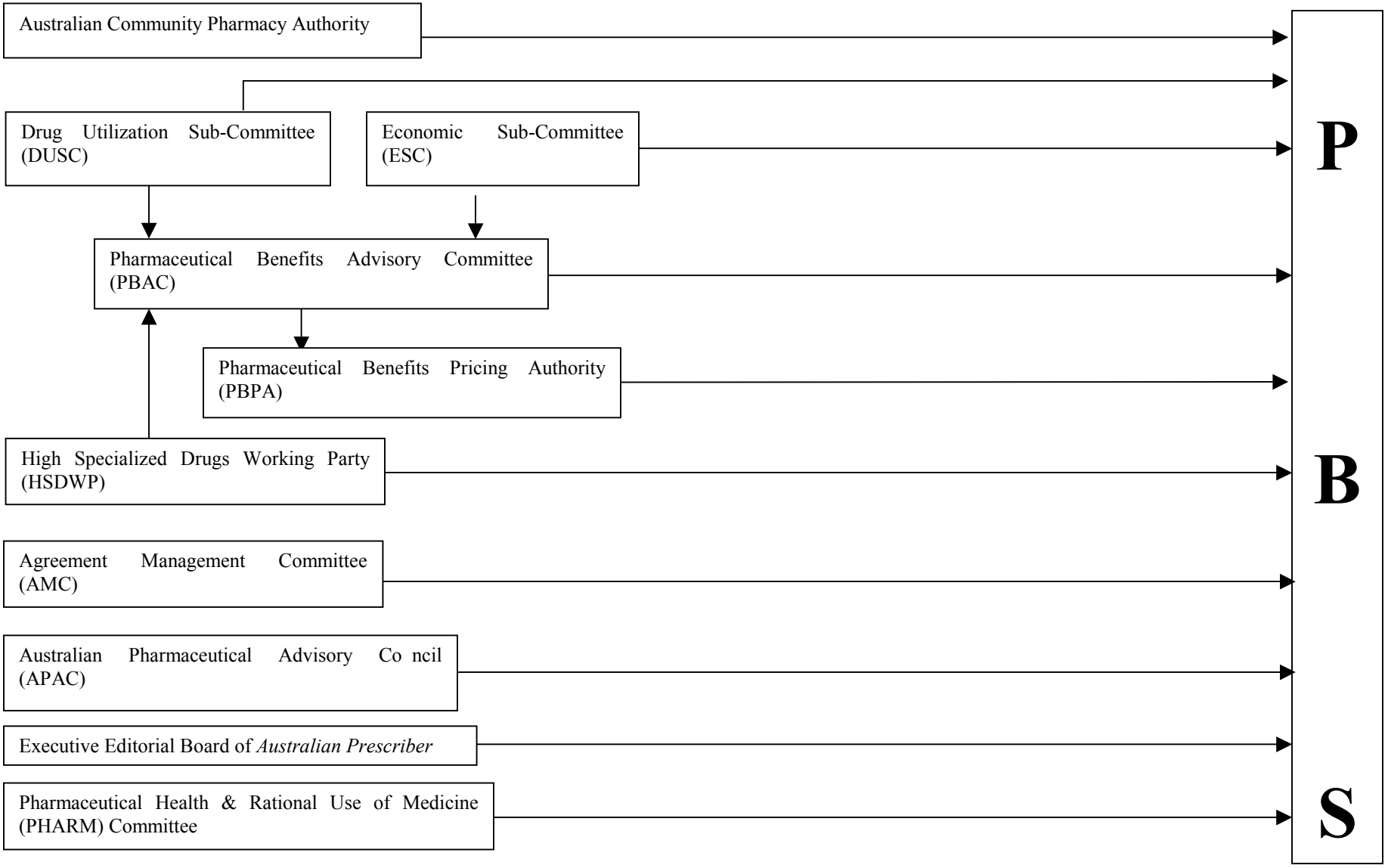
Regarding their post-marketing monitoring program, the PTC planned to conduct cost-effective analyses looking at outcome measures such as length of stay and readmission data, not just mortality, to confirm the positive findings of the published study in their patients. Secondly, a DUE would examine prescribing correlation with the guidelines. In addition to Nebacumab, other drugs such as erythropoietin and G-CSF would be under on-going prospective surveillance.

Interdisciplinary involvement including support from hospital administration was considered to be a crucial first step in addressing the challenges raised by these newer agents. The difficulty of assembling all the required specialists for smaller hospitals was recognized, but this increased the importance of the roles for guidelines and education of health care professionals in this setting. No subsequent follow-up articles were available.

B. TABLES & FIGURES

Figure 1. Pharmaceutical Benefits Scheme (PBS) Organizational Chart

(from email communication, A. Majchrzak, Pharmaceutical Benefits Branch, Department of Health, Australia)



APPENDIX I. INTERNATIONAL: TABLES & FIGURES

Table 1. Final Set of Indicators for PTC

(adapted from Weekes 1998)

	CORE	*COMPLEMENTARY*
PROCESS	▪ Does PTC have clear authority/accountability? ▪ Mission statement, terms of reference, strategic plan? *Do terms of reference include provision for:* ▪ Decision authority re drug availability, use? ▪ Processes for implementation/evaluation of drug policy? ▪ Appeal mechanism? ▪ Conflict of Interest? ▪ Regular meetings? (business addressed within 3 months of receipt) ▪ Operational resources allocated to PTC? ▪ Representatives from each of the following: md's, nurses, pharmacists, expert in therapeutics, community health perspective, societal view? ▪ Decision rationale documented and available to stakeholders? ▪ Drug submission guidelines? ▪ Non-formulary drug requests handled by standard mechanism overseen/ratified by PTC? ▪ Critical review of formulary in past year? ▪ Drug promotion? ▪ Assisting discharged patients in maintaining medication regimen? ▪ Unregistered and alternative drug use? ▪ Reviewing all mortality attributable to preventable ADR or medication errors? ▪ Supporting or endorsement of: • educational info to health workers • objective info to prescribers • audit feedback • continuing ed re therapeutics	▪ Attendance of membership >50% meetings ▪ Proportion of agents on formulary from specific drug group: a) general anesthetics; b) iv cephalosporins. ▪ Proportion of target audience who received specified drug guideline (doctors, nurses)
IMPACT	▪ Percentage of submissions to PTC with a) balanced, comparative info re clinical efficacy & safety; b) economic analysis; c) assessment of clinical need . ▪ Percentage of new drug policies which were adopted	▪ Non-formulary drugs as proportion of total drug expenditures. ▪ Percentage of doctors, nurses reporting use of specified drug guideline. ▪ Percentage of improved compliance with drug guidelines for specified condition following intervention. ▪ Number of ADR/1000 beds per year reported to national database.
OUTCOME	▪ Morbidity rate due to preventable ADR or medication errors.	

APPENDIX I. INTERNATIONAL: TABLES & FIGURES

Table 2. Summary of Guidelines for Pharmacoeconomic Evaluations

(modified from P. Jacobs et al, PharmacoEconomics 3(3) 1995)

Origin	Australia	Canada	Ontario	England & Wales
Purpose	for formulary decisions (listing and pricing)	to inform decision-making for a variety of purposes	for submission for listing as a drug benefit for public funding	to offer NHS purchasers and prescribers information on cost-effectiveness
Comparator	the therapy that most prescribers would replace in practice	all relevant, including 'do nothing'	alternative for same condition, least expensive and most commonly used were emphasized	comparator not specified, but choice must be justified
Type	dependant on objective. CBA not encouraged	CUA preferred. CBA (on experimental basis) preferred.	CUA and CBA (with implications explicitly stated) preferred.	any recognized technique.
Time horizon	appropriate to disease and treatment	Long enough to capture all relevant outcomes	Long term effects emphasized, with the need for modeling recognized.	Full description of treatment path.
Perspective	Social (that includes only direct costs unless otherwise justified.)	Social (presented in a disaggregated fashion)	Social (presented in a disaggregated fashion)	Social (presented in a disaggregated fashion)
Outcome Selection	Appropriate to treatment. Final outcome indicators preferred if life extension is a concern, but may be predicted from intermediate indicators. Use of QOL where appropriate, QALYs not required. Monetary benefits not encouraged.	QOL emphasized. Recommendation of one measure from each of generic, disease-specific, and a preference (utility) measure. Monetary benefits recommended on an experimental basis.	Use of final outcomes and QALYs emphasized. Monetary benefits encouraged, with careful interpretations.	Measures should be identified and justified. Where used, QOL should be measured using 'proven generic' measures.
Method of data capture	High quality randomised trials where possible, with supplemental information from other sources (observational studies, case control, focus groups)	Not specifically addressed, but randomised trials seem favoured	Meta-analysis using randomised trials.	Clinical trials, meta-analysis, observational data, modeling.
Cost items	All direct costs. Indirect costs only where material. A reference source has been developed and is the standard.	All relevant costs in reference to the viewpoint specified. Costs defined as opportunity costs, and include direct, 'spillover' and some indirect costs. Unclear about the cost of patient time.	All relevant costs (direct and indirect) in reference to the health care system.	'Full opportunity costs' including capital and overhead as a proxy for 'long run marginal costs'.
Discounting	5% for costs and outcomes.	Future costs and outcomes at 5% to allow for comparability across studies.	Future costs and outcomes. Acknowledge that the rate most commonly used is 5%.	Costs and outcomes discounted at the treasury rate (currently 6%). Non-monetary outcomes alternatively discounted and not discounted.
Sensitivity Analysis	On imprecise estimates use confidence limits as bounds. On costs replace average by marginal costs.	On assumptions as well as on estimates (i.e. test how the inclusion of cost items, discount rates and other measures influence ratios.)	On utilities and on methodology used to go from clinical effects to values, aim is to assess 'the robustness of qualitative conclusions.'	On all uncertainty in the study. Use of confidence intervals as appropriate.

Table 3. Listing of Drugs Eligible for Public Insurance Reimbursement

Country	Listing of drugs	Comments
Australia	Yes	Listing according to medical needs and cost-effectiveness, updated every 3 months.
Austria	Yes	Listing according to medical and economic criteria. List updated every 3 months to reflect medical and market changes. There is a list of drugs reimbursable without prior approval by sickness funds
Belgium	Yes	List updated every month.
Canada	Yes(1)	Lists and formularies are part of the reimbursement system of provincial insurance plans. The criteria often include pharmaco-economic considerations.
Czech Republic	Yes	The general list of medicines available under prescription is issued by the Ministry of Health
Denmark	Yes	List constantly updated.
Finland	Yes	Listing according to effectiveness of drugs. Constantly adapted.
France	Yes	Listing according to the marginal improvement of health service allowed by the drug and the reduction in costs of medical treatments. Difficulties for proper update.
Germany	Yes(2)	Listing according to pharmacological criteria
Greece	Yes	The list was adapted and implemented in 1989/90, but physicians continue prescribing out of the list, justifying exemptions. Since 1995, a National Committee has the responsibility to adapt the list for all the insurance funds and the NHS. In 1997 a positive list was introduced by IKA and generalized to other insurance funds in 1998.
Hungary	Yes	Listing according to the indication and frequency of the illness.
Italy	Yes	Positive listing introduced in 1978 (Prontuario Terapeutico Nazionale). Important revision and de-listing in 1994 and 1995. Some products readmitted under conditions in 1998. .
Japan	Yes	Listing according to the effectiveness of drugs.
Korea	Yes	Listing according to criteria such as the therapeutic value of drugs, the cost of comparable treatments, and prices observed in foreign countries.
Luxembourg	Yes	List updated monthly.
Mexico	Yes	The list has to cover the existing pathologies at the lowest possible cost. It is adapted based upon medical progress and population health needs
Netherlands	Yes	Listing according to effectiveness. The list is updated regularly.
New Zealand	Yes(3)	
Norway	Yes	Listing according to type and seriousness of disease. Constantly adapted.
Spain	Yes(2)	Listing according to medical criteria, severity and time of the pathology, therapeutic and social use of the drugs; Socio-economic criteria include use of alternative drugs at lower prices, public expenditure fiscal constraints.
Sweden		Lists of recommended drugs set by country councils.
Switzerland	Yes	Drugs listed must be effective, economically efficient and appropriate. Positive list updated twice a year.
UK	Yes	N/A
USA	Yes (HMOs, PBMs)	N/R.

(1) Most of the provinces and territories have established their own formulary for the provincial schemes. (2) Negative list. (3) List of subsidized items only, for reference pricing.

Source: OECD Questionnaire on pharmaceutical management and regulation, and various sources. Used with permission.

Table 4. Drugs in hospitals

Country	Specific rules	Comments
Australia	Yes	Highly specialized drugs requiring monitoring are dispensed through hospitals e.g. drugs for AIDS.
Belgium	Yes	Some specialties are only reimbursed when administered in hospitals. Expensive drugs for AIDS are dispensed by hospital pharmacists for the moment. The hospitalized patient pays a fixed amount of 25 BEF per day for drugs, not depending on the amount of drugs provided.
Canada	Yes	Drugs administered in hospital are part of insured hospital services under federal health care legislation, the Canada Health Act. When in hospital for necessary care, Canadian residents are entitled to medications without financial charges of any kind.
Czech Republic	Yes	In practice, the expensive drugs are usually applied in a specific treatment and are mainly distributed through specialized in-patient facilities. However, in principle, dispensation through outpatient facilities is also possible.
Denmark	Yes	In hospitals, there are specific guidelines for prescription by physicians.
Finland	Yes	High-cost experimental drugs can be dispensed only through hospitals. AIDS medicines are dispensed from public hospitals without any cost for the patient.
France	Yes	Some expensive and particularly innovative drugs are dispensed only by hospitals. However the government has decided that such drugs will gradually be obtainable at a pharmacy with a prescription initiated in hospital. Prices for hospital drugs are free and subject to a biding process. There are calls for tender to supply such drugs and negotiation over prices between hospitals and manufacturers.
Greece	Yes	Expensive medicines (AIDS etc.) and medicines for the poor or unemployed are distributed through hospitals or health centres which are related to hospitals. There is a program recently run for hospital drugs (15% of the drug market) to implement a unit dose (per patient/per day) system to monitor all hospital drug stores.
Hungary	Yes	The extremely expensive but indispensable pharmaceuticals are financed from a separate source of the National Health Insurance Fund Administration, under the auspices of an expert panel. The number of patients treated is limited.
Italy	Yes	A minimum 50 % rebate on the market price is applied to drugs used in hospital settings.
Luxembourg	Yes	Medicines used for in-patient care are completely refundable. Expensive medicines are distributed in hospitals and outside.
Mexico	Yes	Since the public health sector in Mexico has many competing demands for its limited resources, so that in general basic health care is prioritized. For this reason, the availability of these medicines is limited, so that the supply is very far from satisfying the demand. Generally, costly treatments are only available in specialized hospitals, which are only located in highly populated urban area.
Netherlands	Yes	Hospital guidelines on medicine dispensation exist. Individual hospitals receive sometimes subsidies specifically intended to finance expensive medication, such as for the treatment of AIDS.
New Zealand	N/A	Drugs are included in hospital global budgets. Hospital drugs are not subsidized through the reference-pricing regime discussed above.
Spain	Yes	Some drugs are dispensed only through hospitals.
Sweden	Yes	Since 1993, Apotekslaget keeps right to negotiate direct agreement with manufacturers for the price of these drugs.
Switzerland	N/A	The Sickness Law relates only to ambulatory setting. Medicines in inpatient care are included in a global payment a day. Nevertheless ambulatory treatment with very expensive drugs may be started and supervised by university hospitals.
Turkey	Yes	Although, according to certain insurance policy organizations (such as SIO), certain medications should be prescribed only by specialists and be used in hospitals, only blood and some blood products are implemented, dispensed and distributed through hospitals.
UK	Yes	Medicines in hospitals are not covered by the PPRS. Hospital drugs are treated as other inputs to hospital care. Specific drugs are not restricted to hospitals, but while patients are under the care of hospital consultants, the cost of these drugs will fall to hospital budgets. As a consequence some pharmaceuticals - including some for AIDS - will often be prescribed by hospitals. New and expensive drugs need to be limited to the hospital sector with specific arrangements and co-operation between Health Authorities and GPs.

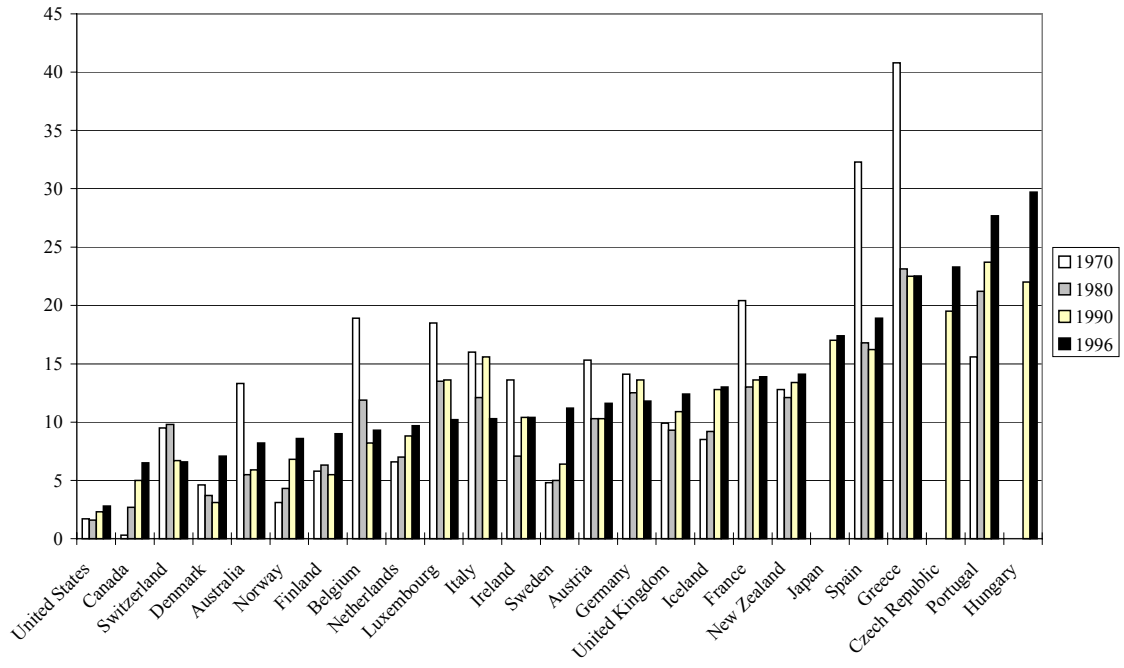
Austria, Germany, Japan, Korea, Norway, Sweden and the United States have no specific rules for drugs in hospitals.
Source: OECD Questionnaire on pharmaceutical management and regulation, and various sources. Used with permission.

Table 5. Guidelines for prescription

Country	Guidelines	Comments	Possible Sanctions
Australia	Yes	Advisory guidelines, including newsletter to prescribers, and feedback to prescribers on their performance against the average. State guidelines also.	No
Austria	Yes	The guidelines apply to the whole range of medical treatment options.	Yes, contractual obligations include refunds or termination of contracts.
Canada	Not at federal level but in most provinces have	Most provinces have a clinical practice guideline activity underway, including prescribing guidelines.	N/A/
France	Yes	Negative Reference Mandatory Guidelines for certain drugs.	Yes, in theory, there are financial and contractual sanctions.
Germany	Yes	In fact, physician prescription is reviewed ex post at the level of sickness funds.	Yes, prescriptions are examined by sickness funds.
Greece	Yes	IKA doctors have to follow the list of drugs and they are reviewed ex-post to detect over-prescribing physicians.	Yes, IKA Board of Directors and the Governor of IKA normally give fines to doctors who over-prescribe and in very few cases fire them.
Hungary	Yes	Therapeutic protocols exist for the treatment of the most frequent pathologies. These protocols suggest effective and cheap medicines.	Yes, financial sanctions from the Insurance Fund Administration.
Japan	Yes	There are guidelines for the treatment of the elderly high blood pressure.	No
Korea	Yes	Guidelines from medical insurance to restrict use of treatments with limited efficacy.	No
Luxembourg	Yes	"Transparency list" and negative mandatory medical guidelines, following the French model.	Yes in theory. R.M.O. guidelines regulation in preparation. Close to the French model.
Mexico	Yes	Therapeutic-Diagnostic guides are distributed to physicians.	No
Netherlands	Yes	Guidelines are set both for general practitioners and specialists. National network of 650 local groups participating in pharmaco-therapeutic consultation.	No, used by the insurers mostly for feedback
New Zealand	Yes	Information is distributed by the pharmaceutical agency to physicians.	No
Norway	Yes	There are broad guidelines	No
Sweden	Yes	Information is distributed to prescribing physicians. (guidelines for 11 common diseases).	No
UK	Yes	Advice issued across a wide range of practices in line with policy towards clinical and cost effectiveness. Relevant professional body also issue advice to their members. Computer aided prescribing system under trial within the NHS should provide detailed information on cost-effectiveness.	No
USA	Yes	There are various publications available for use by physicians. Guidelines are set by managed care organizations.	Yes, according to the type of managed care setting.

At the time of this questionnaire, No data is available for Spain. No guidelines were reported in Belgium, the Czech Republic, Denmark, Finland, Spain, Switzerland, and Turkey. There may however exist in these countries other types of incentives to prescribe cheaper drugs.
Source: OECD Questionnaire on pharmaceutical management and regulation, and various sources. Used with permission.

Figure 2. Public expenditure on pharmaceutical goods as a percentage of public expenditure on health



Source: OECD HEALTH DATA 98. Used with permission.

Table 6. Pharmaceutical Research And Development As A Percentage Of Domestic Sales, In Eight Countries, 1988 And 1995

Country	1988	1995
Canada	6.1%	11.7%
Italy	11.0	11.7
France	15.7	17.2
United States	16.2	18.4
Germany	16.7	20.5
United Kingdom	22.2	25.8
Sweden	32.8	58.1
Switzerland	141.1	47.2

Source: Federal/Provincial/Territorial Task Force on Pharmaceutical Prices (in Menon, 2001).

APPENDIX I. INTERNATIONAL: TABLES & FIGURES

Table 7. Summary of Selected International DT&C Literature

Country	Australia		
Source	*Drug & Therapeutics Committees in Australia: expected and actual performance. Weekes, 1996*	*Indicators for Drug and Therapeutics Committees. Weekes, 1998*	*Drug Use Evaluation: A Selection of Practice Options. NSW TAG (New South Wales Therapeutic Assessment Group, May 1999)*
Format	National Survey + focus groups (1995)	field testing, then consensus panel. Indicators: 35 initially—4 outcome, 7 impact, 24 process. (see attached)	Survey of 25 NSW hospitals, 12 interstate. Response rate 25/37 (68%)
Sample	306 hospitals	field tested in 16 hospitals—only 2 asked declined to participate	not addressed
PTC	>92% (central PTC in one Aussie state:Queensland)	inclusion criteria	
Hospital Types	Teaching, urban non-teaching, regional, rural district, subacute, private	5 teaching, 3 urban non-teach, 4 region/rural, 4 private	
Size	average 9 (range 3-23)		
Meetings	84% reported >50% attendance at most (>60%) meetings	attendance at >50% of meetings?; regular meetings w/i 3 mos of receipt?	
Membership	90+%: internal medicine, pharmacy, nursing 60%: admin <50%: surgery, gp, micro, finance, pharmacology, consumer	reps from the following: mds, nurses, pharmacists, expert in therapeutics, community health perspective, consumers?	
Teaching PTC	significantly higher representation by pharmacologists, DUE pharmacists		
Expectations	best practice, equal access, transparency, consultation; ethics; educational role	clear authority, accountability?	
Main Activities	policy, rational use cost containment, adverse event monitoring, formulary mgmt, education	mission statement, terms of reference, strategic plan? operational resources?	
Main Issues	quality drug use, drug policies, spending on hi cost drugs		
Drug Submission Info/Eval	therapeutic alternative availability (87%), efficacy (83), cost (80), estimated use (78). (Note: s/e & indication not considered by approx 1/3 of PTCs) (rural hospitals signif. less info)	drug submission guidelines? non-formulary drug requests: standard mechanism involving PTC? appeal process? conflict of interest? decision rationale documented/available to stakeholders?	
Implementation/ Monitoring (DUE)	>65%: DUE, medication errors/ADR; much less commonly--infection rates, antimicrobial resistance, readmit rates 60%: Guidelines, prescribing restrictions, clinical pharmacist; 32%: formulary; 38%: restricted drug list; rarely nurse monitoring, critical paths.	decision-making authority re drug availability, use? % of medical staff receiving targeted drug guideline? # ADR/1000 beds? process for implementation/evaluation? critical review of formulary in past year?	1. *TAG recommended the following DUE members*: Physician w DUE interest/clinical pharmacologist; Clinical pharmacist; Nurse; QA and PTC reps; secretarial support *DUE much more likely if* : >200 beds, capital city location, tertiary referral centre *DUE Pharmacist position funding*: pharmacy staff budget (20%); saving salary (8%); medical service/division (8%); no funding (20%); no response (32%) *DUE results most commonly reported to*: Dir Pharmacy (14 hosp); PTC (14); pharmacy staff (11); medical staff (10); Hospital executive & nursing (both 7). *DUE triggered most commonly by*: PTC (14 hosp); pharmacist (12); Dir Pharm (11); DUE pharmacist(9) 6. *DUE time allocated per week* (unclear as reported in survey)
Improve drug use	>90%: education/behavioural—audit & feedback, drug bulletins, presentations	% of staff reporting use of specified drug guideline? % of improved compliance with guideline post intervention? % of non-formulary drugs within total drug budget? educational info to staff? audit-feedback?	not addressed
Effectiveness	able to implement 75% of decisions; teaching hospitals rated higher performance; admin/staff moderate acceptance; patient awareness very infrequent	% of PTC submissions with balanced, comparative info re clinical efficacy & safety; economic analysis; assessment of clinical need? % of new drug policies adopted?	not addressed
Comments	cost-effectiveness data minimally available; poor access to DUE pharmacists, pharmacologists & c-e experts.		

Table 7 (cont)

Country	United Kingdom	
Source	*A review of methods of drug cost management in hospitals. Pacey, 1998*	*Models of hospital drug policy in the UK. Cotter, 1997*
Format	na	focused interviews
Sample	na	8 hospitals, broadly representative of UK NHS hospitals
PTC	in 92% uk hospitals as of 1987 increasingly multidisciplinary cost containment & predicting budget via drug usage formulary development treatment guidelines control over introduction new drugs communication/educational role	**3 models identified:** ***Traditional*** most common hospital-wide drug policy developed in cooperative manner, by multidisciplinary groups (usually PTCs) medical, nursing, pharmacy staff develop policy based on scientific, clinical and financial principles to control costs, encourage rational prescribing new drug permitted for trial period w evaluation clinical value by consultant, pharmacy reviewed literature re effectiveness/cost-effectiveness PTC normally chaired by md or pharmacologist (if one available) drug policy disseminated by formulary local ownership critical: 'importation of a formulary from another hospital, without local involvement, was thought to be a recipe for disaster' formularies initially seen as means to reduce expensive and inappropriate treatments; changing to perspective that many services now under funded drug policies should consider benefit as well as cost ***Combined*** (specialty-oriented variations on hospital-wide model) favoured at hospitals with specialist or directorate pharmacists possibly evolved from traditional model when hi-cost specialties began receiving services from specialist pharmacists, or clinical directorates began to pay for tailored pharmacy service addressed problem of insufficiently detailed info to support decision making disadvantage: focus on directorates could threaten feasibility of maintaining hospital-wide formulary (decreasing cost-effectiveness of purchasing, storage, supply) close relationship between pharmacist and directorate staff felt to enhance credibility of pharmacist, increase role in drug policy/responsibility for drug budgets, improve cost-effective use of drugs ***Medical (out of) Control*** only 1/8 sites specialists need 'complete freedom to develop new therapies' therefore no hospital-wide drug policy or PTC. gradual approach to adoption of formulary, audit, resource management
Hospital Types **Size**	not addressed	not addressed
Drug Submission Info/Eval	pharmaco-economic assessment mandated in Australia, New Zealand and Ontario, but not US or UK. UK encouraging use of economic evaluation with guideline release *(ABPI and Department of Health Guidance on good practice in the conduct of economic evaluations of medicines. 20 May, 1994. Assoc of British Pharmaceutical Industry, London.)* but these guidelines criticized due to minimum consultation with those in the field, little evidence of scientific rigour, little info re monitoring *SOJA technique*: drug evaluation models compare drug characteristics; apply weightings to each attribute based on clinicians' consensus. Score for each drug. Higher score improves likelihood of acceptance onto formulary.	not addressed

APPENDIX I. INTERNATIONAL: TABLES & FIGURES

Country	United Kingdom	
Implementation/ Monitoring (DUE)	1. *Clinical Directorate Pharmacists* (decentralized control) directorates (programs) typically composed of clinical director, business manager, senior nurse, accountant accountable for directorate budget financial impact of directorate pharmacists: saved <90K £ in one year; saved <100K £ by an ICU clinical interventions by ward pharmacists 2. *DUE* (linking health outcomes & interventions to prescribing behaviour) e.g. 1994 survey 733 hospital pharmacists, 374 ID specialists; (50% response rate): restricted lists (75%) cost control campaigns (50%) educational campaigns (50%) therapeutic substitution (45%) auto stop dates (25%) measurement of compliance to formulary only 40%, 10% audit, 10% drug utilization coordinators guidelines, antibiotic policies, program pharmacists, ID consultation, drug purchasing contracts, on-line prescribing all may contribute to improved prescribing antibiotics *(per Tritschler, 1997: How pharmacists can help in rationalizing antibiotic prescribing in hospitals (Hosp Pharm 4:202-204))*	not addressed
Improve drug use	1. *Restricting prescribing* (joint hospital/community formularies) formulary success dep on peer review, continuous prescriber feedback, educational/promotional programs, continuous monitoring, effective PTC. Close collaboration b/w mds & pharmacists, reassessment of formularies. 2. *Purchasing, stock control, waste reduction* reduced drug lines, generic substitution, group purchasing computerized inventory (quantity dispensing, expiry date monitoring, iv additive systems?) use of patient's own meds during admit 3. *Therapeutic Substitution* (more recently in UK than US) US programs included: H_2RA, vitamins, antacids, antibiotics 4. *Treatment Guidelines* 5. *Drug Cost information* commonly in large hospitals provided to physicians, clinic directors via directorate pharmacists monthly prescribing/cost feedback	not addressed
Effectiveness	not addressed	not addressed
Comments	*NHS Changes* (designed to increase delivery of cost-effective health care): 1989: NHS restructured due to white paper, *"Working for Patients":* encouraged self-governing trusts and policy approval for resource management. Clinical directorates formed within hospital management, decentralized drug budgets to directorates. 1991: NHS R&D to phase out ineffective treatments and encourage evidence-based practice. 1992: *Cochrane Collaboration UK Centre* created; *health outcomes group* also est'd by Dept. of Health 1994: *Purchasing & Providing* (NHS) 1996: *Improving Clinical Effectiveness* (NHS): encouraged strategic guideline development & comparison of health care interventions in particular drug therapies.	

Table 7 (cont)

Country	The Netherlands	
Source	*Drug and Therapeutics committees in Dutch hospitals: a nation-wide survey of structure, activities, and drug selection procedures. Fijn, 1999*	
Format	Survey sent to hospitals w following inclusion criteria: >300 beds PTC w written statute and printed hospital drug formulary Survey based on Australian Indicators (Weekes 1998)	International Comparisons (noted within above article)
Sample	54 hospitals met criteria (including 7 teaching); 70% response rate (w/i 3 month time limit)	
PTC	All (part of inclusion criteria)	PTC established in 1930s in US; 1984 Dutch legislation req'd PTC including at least one pharmacist, clinician and nurse PTC in 98% of all general hospitals; 89% w written statute (similar to other countries)
Hospital Types	30 (80%) responsible for 1 institution 8 (20%) responsible for others (range 1-9): nursing homes, psych, other specialized hospitals 23 (60%) subcommittees (range 1-20) including: antibiotics, antithrombotic therapy, drug distribution, nutrition, blood products, psychotropic meds, expensive drugs, HDF editing, development of pharmaco-therapeutic guidelines	
Size	avg 8 (3-14); selection by general board of hospital management for 1-3 yrs.	PTC numbers similar to Ireland, median 7 (2-12); US—10 (8-12) (1986, 1993) different from Germany, med 12 (5-40) (1997)
Attendance	65% met at least bi-monthly; <10% quarterly, once/twice annually or irregularly 55% restricted meetings to members	
Membership	hospital pharmacists secretary in 95%, chair in 35% pharmacists present in 100%; internists (95%); other med specialties (≤55%), although often represented in subcommittees; nursing, (30%) clinical pharmacologists in ¼ of PTCs	clinical pharmacologists underrepresented (as in other countries e.g. Australia 1996, Germany 1997)
Teaching PTC	not addressed	not addressed
Expectations	not addressed	not addressed
Main Activities	Theoretical (noted in PTC statutes) vs. Actual responsibilities: comparable—general prescribing policies; drug selection and HDF editing; pharmacotherapeutic quality of care; disparate—HDF compliance and compliance to other policies (Theory: 90% v Actual: 55%); medication surveillance (T: 50% v A: 25%); drug expenses (T: 20% v A: 75%)	*Model Statute* (Dutch Assoc Hosp Pharmacists , ASHP (1989)—PTC responsible for: HDF important role re pharmacotherapeutic policies efficient drug distribution drug info/education DUE Dutch pharmacy staff frequently bear sole responsibility for communication, advice, policy, monitoring, regulation theoretically Dutch PTC not responsible for drug expenditures, however often Hospital Boards of Management have informally passed on this responsibility. Dutch PTC, unlike other countries, are not involved in educational activities

Country	The Netherlands	
Drug Submission Info/Eval Process (DUE)	50% mandatory procedures for HDF submissions but only half of these had printed forms. info required in >95% PTCs: original clinical research articles regional/national pharmaco-therapeutic treatment guidelines clinical reviews, commentaries, case reports info from (sub)governmental agencies product info from drug manufacturer many PTCs not familiar with meta-analysis generally therapeutic considerations favoured over practical, economic, organizational factors 37 (95%) familiar w decision supportive selection matrices (e.g. SOJA-System of Objectified Judgement Analysis). Only 15% actually used matrices. 85% felt them complex, time-consuming or manipulable. 16 (40%) considered pharmacists to have highest impact on drug selection; 15 (40%) pharmacotherapeutic clinical experts; 7 (20%) internists. 26 (70%) PTCs mainly replaced drugs on HDF; 9 (25%) mainly added drugs. avg 15 drugs added to HDF annually (range 10-25). [30 new drugs introduced to Dutch market annually] Specialties most difficult to achieve consensus: cardiology (45%); internal med (30%); psych (25%); anesthesia (20%). Most complex drug groups: cardiovascular (45%); antiemetics (35%); radiol. contrast agents and antidepressants (both 20%); 40% PTCs did not consider any drug group more complicated than another. in cardiology, int med & psych wide variety of equally effective meds available; individual experience, education, & drug company marketing strategies considered high impact in forming opinions of clinicians in these areas. psychiatrists reluctant to choose one drug over another due to pressure from patients and patient organizations; also clinical outcomes varied considerably for individual drugs in individual patients all PTCs recognized marketing strategies of drug companies conflict of interest policies: 35% absolute transparency 55% declaration only required for few drug groups 10% no policy 2. 45% mentioned industry influence demonstrated by incomplete/biased clinical data presented at meetings, and 'deviant prescribing behaviour' in outpatient depts.	procedures and evaluation of HDF drug application/selection similar to other countries; lack of transparency in drug selection (lack of decision supportive matrices) need for evidence-based and pharmacoeconomic information generally accepted. Dutch PTC prefer to react to requests from clinicians rather than be proactive (horizon scans etc) pharmacist has greatest single involvement and influence on drug selection (similar to other countries) Hospital Management Boards in Netherlands only tend to be involved with very expensive drugs.

Table 7 (cont)

Country	United States		
Source	*Mannebach, M 1999 Activities and Structure of PTC in large teaching hospitals*	*Campbell, G 2001 The state of drug decision-making: Report on a survey of PTC structure and practices*	*Motheral, B 2000: Role of pharmacoeconomics on drug benefit decision-making: results of a survey.*
Format	1995 survey	survey comprised of 3 subsurveys, March/April 2001: 1) PTC and subcomm structures, influences on drug decision-making 2) formulary decision-making 3) PTC activities, future directions	3 independent subsurveys, Dec 99/Jan 2000: 1) use/import of pharmoeconomic info; 2) sources of p-e info; 3) internal research activities and barriers to use of p-e info.
Sample	187 US hospitals (70% response rate)	random mailing to 1000 formulary journal subscribers for each subsurvey; overall response rate 30%; responders: 80% PTC member; 10% PTC contributors; 10% previous PTC members.	random mailing to 3000 from pool of 6000 Formulary Journal subscribers who were physicians or pharmacists in MCO; response rate only 14%
PTC	inclusion criteria	inclusion criteria	inclusion criteria
Hospital Types	all large teaching	independant hospital/health system, 70%; MCO, 10%; LTC/pharmacy provider, 8%; govmt agency, 5%	100% MCO
Size	~1/2 had 500-750 beds; 1/3 <500; mean medicare case mix index of 1.7 ('relatively complex conditions'); mean LOS 6 days	not specified	not addressed
Meetings	about 10/yr, 80 min each	75% meet quarterly or monthly; most subcomm meet as needed, but over 1/3 meet quarterly/monthly	
Membership	avg 19 (90% voting); 12/19 mds, 3/19 pharm, 2/19 nurs, 1/19 admin	avg 13 (45% ≤10, 30% 11-15; 10% >20); avg term 4 yrs; subcommittees: 50% none; 45% 1-5; 5% 6-10; most common, antibiotic/ID: 70%; CV: 30%; guidelines/critical paths: 25%; drug errors/ADR: 20%; hem/onc: 15%; prim care: 15%; peds 10%; gi 10%; drug contract negotiations: 10%. UR/QA officers on majority; pharmacoeconomists, outcomes measurement analysts <20%, but these along with info technology specialists and patient privacy officers most likely additions in next 2 yrs.	survey respondents: 75% pharmacists; 70% attended continuing ed course on p-e; worked in health care for avg 20 yrs.
Teaching PTC	inclusion criteria	not specifically addressed	not addressed
Policies	about 70% had formal therapeutic interchange policies; 2/3 included requestor in decision-making process; ½ had formal conflict of interest—10% with policy to prohibit drug reps from contacting PTC members	drug use ethics policies, 20%	not addressed
Main Activities	major issues: formulary control-45%; DUE-30%; review drug use p&p-20% formulary maintenance: 90% had closed formulary; 18 additions/16 deletions annually study compared consistency of 3 major drug classes: po H2RA, statins, ACEI H2RA: 2 +-1 (all 4 with similar frequency on all formularies) statins: 2 +-1 (lovastatin 80%) ACEI: 3 +-1 (most had captopril & enalapril, plus one additional ACEI)	>70% PTC involved in (more commonly in indep hosp/health systems than MCOs) the following: report/monitor ADR/med errors; formulary inclusions/reimbursement decisions; develop/review tx guidelines/protocols; develop drug use p&p; conduct/approve DUE other major activities: 65%, drug use staff education; 55%, eval short-term medical savings for drugs under formulary review; 45%, dev/rev disease management programs; 40%, formulary appeals process horizon scans in about 30%	
Influences	not addressed	Internal (on PTC): pharmacy/formulary director, staff md, medical director, Clinical pharmacy specialist, Drug info officer, pharmacist (more influence in MCO than independ hospitals/systems); nurs, pharmacoeconomist, CEO only some or very little influence. External (to PTC): pharmacists, then mds (drug reps not included)	

Country	United States		
Drug Submission Info/Evaluation	formulary review written by (multiple individuals may contribute): DI pharmacist (55%); clinical pharmacist (45%); pharm admin (15%); physician (3%) formal economic analysis >1/2 reported formal economic cost analysis or cost impact evaluation at least most of the time; 15% reported seldom or never formal econ analysis info in formal economic cost analysis: drug acquisition costs (100%); alternate therapy cost analysis (70%); direct medical costs (55%); substantial minority included indirect costs, resource impact, nonmedical costs "it was not clear whether [PTC] decisions were based on economic, safety, efficacy or other factors".	most significant factors considered (assuming efficacy and safety are top factors): potential for ADR/interactions, impact on QOL, impact on total tx costs, acquisition price, impact of LOS, patient restrictions drug assessment: 50%, comparison with drug(s) the new drug would replace; 40%, review whole drug class; <10%, review new drug on own merits. most frequent scenarios: 'me too' drugs added only if less expensive; weighing nonpharmacy savings/costs; acquisition cost more likely predominant factor in 'preferred/nonpreferred status' decisions than in formulary inclusion decisions. coordination of decision-making: 40% with other facilities; 25% with release of guidelines from national medical associations/organizations. initiating drug evaluation: most commonly after md request and FDA approval; more likely to begin at pre-FDA approval stage if anticipated to be 'budget-buster'; period of 'real-world use' more likely if lifestyle drug, media-hyped or 'me-too' drugs; most commonly delayed if 'me-too' or new indications/formulations of existing drugs.	All ratings: 1 not import-5 extremely important avg importance of factors considered: safety=efficacy=4.8; cost=4.1; p-e=3.9; QOL=3.8; md demand=3.3; rebate arrangement=3; consumer demand=2.6. p-e considered somewhat or very important in 97% managing drug benefit p-e info considered in most or every benefit decision in 50% formulary drug selection most common activity utilizing p-e info most important types of p-e info were studies demonstrating short-term medical savings & those showing higher cost/better outcomes cost-effectiveness and cost benefit analysis were most familiar/useful to 95+% respondents; cost-utility and cost-consequency analysis least familiar/useful re major approaches to p-e analysis: most familiar with clinical studies, less with claims data, least with decision-analytic models (usefulness rated in the same order) p-e info rated more important for these drug classes: antidepressants and cholesterol-lowering drugs, 4.3; gi drugs, 4.1; bp, asthma and dm meds, 4. p-e info sources most useful: peer-reviewed published research, 4.6; professional meetings, 3.8 (least useful, drug ads, 1.5) 40% respondents conduct in-house p-e studies
Implementation/ Monitoring (DUE)	methods not addressed	major triggers of formulary changes: available generic equivalent; addition of equal efficacy, less costly drug. least likely trigger: new or heavily promoted drug which is equally effective, and costly. DUEs in 75% of respondents (more likely in government)	frequency of p-e info affecting decisions: 2/3 respondents said only occasionally; 15% rarely, never.
Improve drug use	primary communication of PTC decisions via newsletter other mechanisms not addressed	improve medication compliance (30%); prescriber feedback (30%): both more common in government settings. drug use education programs for staff (65%)	not addressed
Effectiveness	not addressed, but noted lack of a standard for assessment	not addressed	
Comments	survey based on generic model of group activity proposed by *McGrath,1984* (input-process-output); modified by *Hackman '87,'92* and *Levin & Moreland '90*	PTC influence and regulatory scrutiny expected to increase in next 2 yrs; no change in consumer or employer scrutiny LTC (10% of respondents) more likely to: have PTC <10 members; pharmoeconomist; review a new drug in context of entire drug class; consider QOL; drug's dosing frequency, formulations/strengths. govmt (6% of respondents) more likely to: be influenced strongly by clinical pharmacists; coordinate decision-making with other facilities and release of guidelines; emphasize role of drug costs in decision-making; conduct DUEs; programs to improve compliance; profile physician prescribing. *AMCP* (Academy of Managed Care Pharmacy) Format for Formulary Submissions, 2000s: obstacles to planned implementation included preparation, time, pharmacoeconomic expertise, technological capabilities.	extremely small response rate although total of over 400 respondents: ?representative of the readership/MCOs no standard deviation/medians reported

Table 8. Measures to manage pharmaceutical budgets
(from Willison et al, 2001)

Approaches		Sweden	UK	Germany	Nether-lands	France	New Zealand	Australia
Direct	**Price Regulation (direct and indirect)**							
	Direct price regulation	√ [a]	(√) [b]	(√) [b]	√	√ [a]		
	International price comparisons	√			√	√		
	Profit regulation		√					
	Price-volume agreements					√	√	√
	Advertising expenditure restrictions					√		
	Tendering						√	
	Limiting products for reimbursement							
	Positive lists	(√) [c]				√	√	√
	Negative lists	√	√	√				
	Inducing price competition							
	Generics							
	Automatic substitution	(√) [d]	√		(√) [d]	(√) [e]		√
	Promotion of generic prescribing		√√	√	√√	(√√) [f]		
	Therapeutic reference-based pricing			√	√√		√√√	√
	Use of formal pharmacoeconomic analysis	√	√ [g]		√		√	√
Indirect	**Prescriber-focused**							
	Budgets for pharmaceuticals							
	Collective level		fixed [h]	fixed [i]			mixed [J]	
	Individual level		indicative	indicative [i]				
	Educational programs							
	Clinical practice guidelines	√	√	√	√	√	√	√
	Audit and feedback	aggregate	√	√				
	Electronic medical record	√	√		√			
	Academic detailing		(√)		√		(√)	
	Consumer focused							
	Cost sharing	√	(√) [k]	√	√	√	(√) [l]	√
	Rx to OTC and drop from public reimbursement	√	√	√	√		√	√
	Industry focused							
	Risk sharing					√	√	√

APPENDIX I. INTERNATIONAL: TABLES & FIGURES

Table 8. Legend:
A check (√) is provided if the policy instrument is used in the country. If the check is in paretheses there is some condition or exception, which is explained in the footnote. For "promotion of generic prescribing", 2 checks means that generic prescribing is very heavily promoted. For "therapeutic reference-based pricing", one check indicates limited; 2, moderate; and 3, very heavy use.

---

[a] Manufacturers are free to set their own prices. However, if the product is to be reimbursed in the public insurance program, the reimbursement price must be negotiated with the government. The same price must be used in both the public and private sector transactions.

[b] Officially, the UK and Germany have free pricing of patented pharmaceuticals. However, they have implemented price cut-backs in the 1990's.

[c] There is no positive list at the national level. However, many County Councils have developed their own positive lists.

[d] No formal legislation or regulations authorizing automatic substitution, but physicians and pharmacists frequently have informal agreements for auto-substitution.

[e] Although automatic substitution laws are in place, generics occupy less than 10% of prescription sales.

[f] Generic prescribing is heavily promoted but generics occupy less than 10% of prescription sales.

[g] Pharmacoeconomic analysis limited to subset of products reviewed by the National Institute for Clinical Excellence (NICE).

[h] Primary Care Groups (PCGOs) now hold fixed unified budgets from which hospitals, community health services, community prescribing costs, and general medical services are funded. This allows for the cross-subsidization across budget envelopes that, formerly, had been disallowed. The degree of control over funds will depend on which of the 4 levels of responsibility they have achieved in the transition to Primary Care Trusts. *(Majeed A, Malcolm L. Unified budgets for primary care groups. BMJ 1999;318:772-776)*

[i] In Germany, regional collectives are assigned fixed budgets and individual physicians are assigned indicative budgets. Under fixed budgets, there is no reward for coming under budget but there are financial penalties for over-spending. However, efforts to recover costs resulting from exceeding the budget have never been realized, to date.

[j] Not all primary care organizations (PCOs) have entered into agreements for prescribing budgets. Of those that have entered into contracts, one large PCO has a fixed budget. The remainder have indicative budgets. Under fixed budgets, the PCO accepts 100% of the liability and retains 100% of any under spending. Under indicative budgets, PCOs are advised of the cost over-run but are not held financially liable. However, if the PCO comes in under-budget, it must share 50% of the savings with the government. In the cases of both fixed and indicative budgets, surplus funds retained must be re-invested in the services provided by the PCO.

[k] 85% of prescriptions dispensed are exempted from co-payments.

[l] Although the co-payments in the public insurance scheme are quite large, the intended effect of inducing price sensitivity are lost because most of the population purchase private supplemental insurance (Mutuelles) that pays for the co-payment. In January, 2000, concessions for low income residents were introduced but there may still be a financial barrier for the working poor, as there is a fixed cut-point for eligibility for subsidy as opposed to a sliding scale.

Table 9. Share of US HMOs with closed formularies

HMO Type	*% closed formularies*
Staff model	66.7
Group model	53.8
Independent Practice Association model	38.7
Network model	40.0
Overall	**47.8**

Managed care organization with open formularies impose no penalty to the enrollee for getting a prescription that is not on the formulary. Managed care organizations with closed formularies do. The staff model HMO is the more traditional and vertically integrated model of managed care, while the Independent Practice Association and network models are looser forms of managed care. The group model is intermediate. (No absolute numbers given in original table.) *Source: Datamonitor, CibaGeneva Pharmacy Benefit Report.*

APPENDIX I. INTERNATIONAL: TABLES & FIGURES

Table 10. International Resources

Country	*Resource*	*Type*	*Persp*	*Date*
Australia	Preparation Of Submissions To The Drug & Therapeutics Committee : A Template *(Economic Working Party of the NSW Therapeutic Assessment Group Inc. 1997)*	Templ	Inst	1997
	Manual of Indicators for Drug and Therapeutics Committees—NSW TAG	Manual	State/ Inst	1996
	Manual of Indicators for Quality Use of Medicines—Commonwealth Dept. of Human Services and Health	Manual	Nat	1995
	Manual of Indicators for Drug Use in Australian Hospitals—NSW TAG	Manual	State/ Inst	1998
	Drug Usage Evaluation: A Selection Of Practice Options--NSW TAG May 1999	Guide	Inst	1999
	Guidelines for the Pharmaceutical Industry on the Preparation of Submissions to the Pharmaceutical Benefits Advisory Committee	Guide	Nat	1992, rev. 1995, 2000
	Commonwealth Department of Human Services and Health. 1994. *Manual of Indicators to measure the effect of initiatives under the Quality Use of Medicine arm of the National Medicinal Drug Policy.* Canberra.	Manual	Nat	1994
Canada	Ontario Guidelines for Economic Analysis of Pharmaceutical Products *(Toronto: Ontario Ministry of Health; 1994)*	Guide	Prov/Nat	1994
	CCOTHA Guidelines for economic evaluation of pharmaceuticals (2nd ed. 1997)	Guide	Nat	1997
Intern'l	Indicators for Monitoring National Drug Policies—WHO *(P Burden-Jakobowicz et al)*	Indic	Inter	1994
New Zealand	Pharmaceutical Management Agency (PHARMAC). Operating policies and procedures of Pharmaceutical Management Agency Ltd. (*Wellington, New Zealand: PHARMAC; 1993.)*	Guide	Nat	1993
	Prescription for Pharmacoeconomic Analysis *(PHARMAC Sept 1999)*	Guide	Nat	1999
Switz.	Manual for the Standardization of Clinical and Economic Evaluation of Medical Technology *(Bern: Federal Office of Social Security; 1995)*	Manual Guide	Nat	1995
UK	Guidance on good practice in the conduct of economic evaluations of medicines. (*ABPI & NHS Department of Health)*	Guide	Nat	1994
	Guidelines for authors and peer reviewers of economic submissions to the BMJ *(Drummond et al, BMJ 1996; 313: 275-283.)*	Guide	Inter	1996
	The prescribing of costly *medicines* (Working Party Reports: RCP London: updated October 5, 2000)	Guide	Nat	2000
USA	Task Force on Principles for Economic Analysis of Health Care Technology. *(Annals 1995; 123:61-70*)	Guide	MCO	1995
	Guidelines for Formulary Submissions *(Langley PC et a, Rancho Cordova, Calif: Foundation Health and Integrated Pharmaceutical Services; 1997)*	Guide	MCO	1996
	Guidelines for the Submission of Clinical and Economic Data Supporting Formulary Consideration *(Seattle, Wash: Regence Washington Health; 1997)*	Guide	MCO	1997
	Guidelines for Formulary Submissions for Pharmaceutical Product Evaluation *(Denver, Colo: BCBS of Colorado and Nevada; 1998)*	Guide	MCO	1998
	Format for Formulary Submissions *(AMCP)*	Guide	MCO	2000
	Managed care guidelines for the economic evaluation of pharmaceuticals. *(Langley PC et al Am J Manag Care 1997 Jul;3(7):1013-21)*	Guide	MCO	1997
	Pharmacoeconomic Evaluations: Guidelines for Drug Purchasers *(Langley PC et al, J Manage Care Pharm 1996;2:671-77)*	Guide	MCO	1996
	American Society of Hospital Pharmacists. ASHP guidelines on formulary system management. *Am J Hosp Pharm*. 1992; 49:648–52.	Guide	MCO	1992

Guide=guidelines; Inter=international; MCO=managed care organization; Nat=national; templ=template;

APPENDIX II. CANADIAN

A. ADDITIONAL INFORMATION

Table 11. Canadian National *PTC*s

Organization	**Federal PTC (NIHB Program)**	**National Drug Scheduling Advisory Committee (NDSAC)**	**Therapeutic Products Programme (TPP): Expert Advisory Committee on Pharmacovigilance**	**Review of TPP Cost Recovery Initiative (KPMG, 2000)**
Source	internet	internet (organization established in 1995 by National Association of Pharmacy Regulatory Authorities (NAPRA))	internet	internet
Size	6 (as of July 2000)	7	Core (permanent): up to 8 (2-4 yr term, max 6 yrs Ad Hoc: invited to serve for a specific topic/group of topics for a defined term (term up to 3 yrs)	na
Attendance	4 meetings annually	up to 4 annually mandatory attendance at least ¾ meetings per calendar yr; no absence in 2 consecutive meetings		na
Membership	*Committee:* 4 MDs, 2 Pharmacists (members serve 2-3 yrs) *Department Reps:* 7 (defense, correctional services, VA, RCMP, Can Pub Health Assoc, Citizenship & Immigration, Non-Insured Health Benefits Health Canada. *Resource staff:* 4	Members selected w Canadian expertise in: pharmacotherapy, drug utilization, drug interactions/toxicity, pharmacy practice, academic research, the drug industry, pharmaceutical regulation at federal and provincial levels. Consumers' Association of Canada also represented.	Dir Gen selects chair & core members with expertise encompassing: medicine, pharmacy, basic & applied biomedical sciences, pharmacoepidemiology, ethics, communication of health issues individuals do not represent their organizations Health Canada staff may only serve as observers not members	na
Primary Activities	review new drugs at request of participating departments recommendations directed to dept heads for final decision	advise provincial pharmacy regulatory authorities relating to placement of drugs within a 3 schedule/4 category national model	Responsibilities include: reports to Dir General, Drugs Directorate evaluations of post-approval drug safety, quality, efficacy, effectiveness recommendations for research and educational programs both for professionals or consumers adherence to conflict of interest policy (avoid even appearance of c. of i.)	▪ "Cost recovery is a federal government policy initiative that requires government departments to consider charging appropriate fees for qualifying services. It is a means of transferring some or all of the costs of a government activity from the general taxpayer to those who more directly benefit from or who 'trigger' special activity. " ▪ implemented in fiscal yr 94/5 ▪ cost recovery fees generated from regulatory and related activities in the following 4 areas: o authority to sell drugs o *drug evaluation* o establishment licensing o medical devices
Drug Submission/Eval'n Process (DUE)	approval by Health Canada clinical studies in peer-reviewed journals comparing product to current therapies clinical data should demonstrate efficacy, toxicities, advantages/disadvan of drug complete bibliography search strategies current pricing pharmacoeconomic eval'n conforming to OMH/CCOHTA guidelines showing benefit related to cost and alternative therapies	conflict of interest guidelines meetings generally held *in camera*		na
Comments				may be avenue to help subsidize cost of Central PTC.

APPENDIX II. CANADIAN: ADDITIONAL INFORMATION

Comparisons of Drug Expenditure in Retail Establishments and Hospitals
(from 'Drug Expenditures in Canada, 1985-2000. CIHI (2001))

Trends—1985 to 1998

Drug expenditure in retail establishments grew by over 10% in each year between 1985 and 1992. The annual increase of drug expenditure in hospitals was also above 10% until 989. However, the increase moderated substantially in subsequent years and was only 3.3% in 1992.

During the period 1992 to 1996, drug expenditure in retail establishments grew annually at rates ranging between 2.5% and 10.6%. In the same period, the annual rate of change of drug expenditure in hospitals was considerably lower, ranging between 1.1% and 3.3%.

In 1997, the increase of drug expenditure in retail establishments was again above 10%, while drug expenditure in hospitals rose by 5.6%. Contextually, restructuring and downsizing in the hospital sector resulted in 23% fewer (almost 40,000) hospital beds in the health care system between 1993/94 and 1997/98. The bed reductions were offset to some degree by length of stay reductions (i.e. increasing throughput per bed) and substituting outpatient care for inpatient stays. Still, the data above suggest a shift in drug expenditures from hospitals to the community. Drug expenditure in retail establishments was $12.4 billion in 1998, an increase of 9.5% over 1997. By comparison, the increase of drug expenditure in hospitals was much lower at 3.5%. Drug expenditure in hospitals was an estimated $988 million in 1998.

Outlook—1999 and 2000

Drug expenditure in retail establishments is forecast to have reached $13.5 billion in 1999 and $14.7 billion in 2000, increases of 8.9% and 9.0% respectively. The increase for drugs dispensed in hospitals is expected to have been relatively moderate at 4.4% and 2.6%, with expenditures reaching $1.03 billion in 1999 and $1.06 billion in 2000.

Between 1985 and 2000, drug expenditure in retail establishments is expected to have increased by 288%, more than twice the percentage increase of drug expenditure in hospitals (131%), as illustrated in Figure 3.

APPENDIX II. CANADIAN: ADDITIONAL INFORMATION

Table 12. Drug Expenditure in Hospitals, Canada, 1985-2000.

Drug Expenditure in Hospitals, Canada, 1985 to 2000[10]

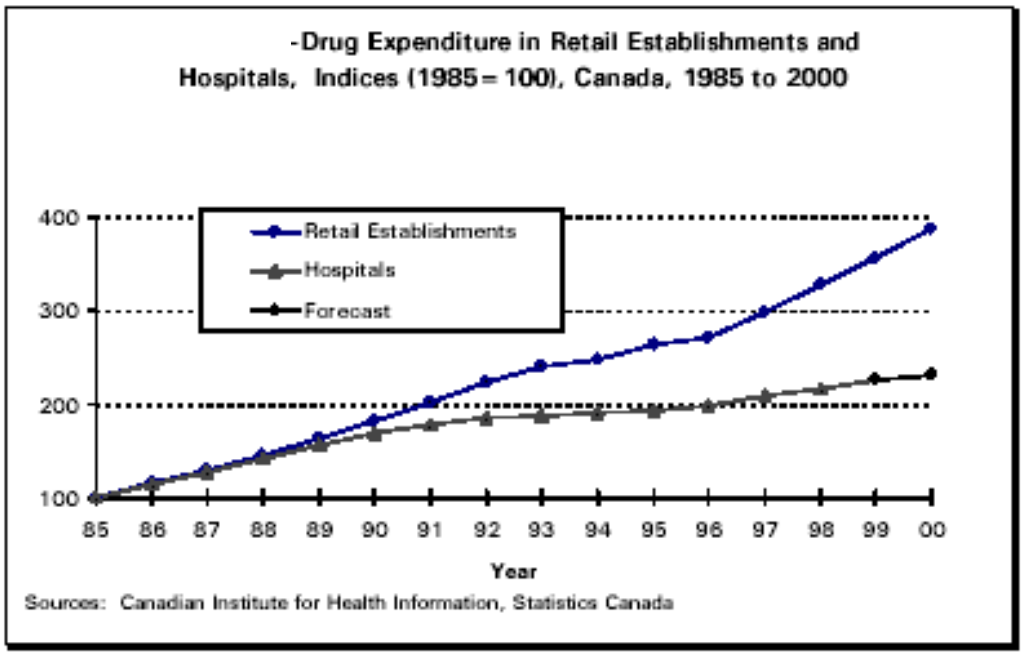
	Total Drug Expenditure		Total Drug Expenditure Per Capita		Share of Total Hospital Expenditure
	($' 000,000)	Annual % Change	($)	Annual % Change	(%)
1985	457.4	---	17.70	---	2.8
1986	522.2	14.2	20.01	13.0	3.0
1987	586.2	12.3	22.16	10.8	3.1
1988	650.1	10.9	24.26	9.5	3.2
1989	715.0	10.0	26.20	8.0	3.2
1990	774.5	8.3	27.96	6.7	3.3
1991	817.6	5.6	29.17	4.3	3.2
1992	844.6	3.3	29.77	2.0	3.2
1993	859.4	1.8	29.94	0.6	3.2
1994	875.0	1.8	30.13	0.6	3.3
1995	884.9	1.1	30.15	0.0	3.4
1996	903.6	2.1	30.45	1.0	3.5
1997	954.4	5.6	31.83	4.5	3.7
1998	987.7	3.5	32.65	2.6	3.6
1999 f	1,030.8	4.4	33.80	3.5	3.6
2000 f	1,057.8	2.6	34.40	1.8	3.5

f- Forecast

Sources: Canadian Institute for Health Information, Statistics Canada

[10] Drug expenditures in Table 2 include only the cost of the drug supplied. They do not include associated costs of hospital pharmacy pertaining to the requisitioning, storage, control, compounding, standardizing, distribution, and monitoring of drugs, and for acting as an information source on all pharmaceutical matters. The full cost of hospital pharmacy cannot be identified in the Annual Hospital Survey. While direct expenses of hospital pharmacy are reported, indirect expenses (e.g. housekeeping, heating, electricity, plant maintenance, capital related costs) are generally not allocated to hospital pharmacy in the survey.

Figure 3. Drug Expenditure in Retail Establishments and Hospitals, Canada, 1985-2000



B. TABLES & FIGURES

Table 13. Canadian Provincial External Advisory Committees (EAC)—Composition

(adapted from Bacovsky Report,1998 and Anis, 2001)

Prov	*UC*	*Sr*	EAC	*MD*	*RX*	*Ph*	*Ec*	*Gv*		*Adm*	*Ben*	*Bio*	*Chm*	*Den*	*Epi*	*Law*	*Nurs*	*Phk*	*Vet*	*Oth*	N	Freq
ON	√	*.40*	***Summary***	√	√	√	√	√							√					√		
			DQTC	√	√	√	√	√							√					√	12	q mo +
BC	√	*.50*	***Summary***	√	√	√	√	√				√	√		√	√			√	√		
			TI	√	√	√									√	√					20	q mo
			PISC	√	√	√	√	√				√			√						14	q 6wk
			PDBC	√	√		√	√														6-10/yr
			RBPEAC	√	√		√													√		q mo
			DAC	√	√			√					√						√		12	q6-8wk
AB		*.61*	***Summary***	√	√	√	√	√										√				
			ECDQ&T	√	√	√	√	√													6	6/yr
SK	√	*.19*	***Summary***	√	√	√	√	√												√		
			SDQAC	√	√	√		√												√		8-10/yr
			SFC	√	√	√	√	√												√		6-8/yr
MB	√	*.39*	***Summary***	√	√	√		√		√							√					
			MDSTC	√	√			√													6	6-8/yr
			PGC	√	√			√		√							√				10	3/yr
			ACSAHSDP	√		√		√													6	8-10/yr
QC	√	*.36*	***Summary***	√	√	√	√	√														
			CCP	√	√	√	√	√													7	q mo +
			CRUM	√	√																≤ 9	
NB		*.36*	***Summary***	√	√			√			√			√?			√			√		
			PDPAUC	√	√			√			√						√				11 *	5/yr
			PSC	√	√			√						√							8	4-5/yr
NS		*.65*	***Summary***	√	√	√		√						√						√		
			FMC	√	√	√		√												√	4	q mo
			D&TC	√	√	√		√						√				√			8-12	q mo
PE		*.50*	***Summary***	√	√	√		√												√		
			PAC	√	√	√		√												√	7	4/yr +
			PBC	√	√			√												√	2+	2/yr
NF		*.40*	***Summary***	√	√			√												√		
			NLPDP (NIDPFC)	√	√			√												√	5	2/yr

Legend: *Adm=administrator; Ben=beneficiaries; Biostats=biostatistician; Chm=chemist; Den=dentist; Ec=economist; epi=epidemiologist; Freq=meeting frequency; Gv=government rep; Law=lawyer; MD=physician; mo=month; N=voting members; Nurs=nurse; NV=non-voting members; Oth=other experts as needed; Phk=pharmacokineticist; Ph=pharmacologist; q=each; RX=pharmacist; Sr=senior ratio (number of active senior recipients relative to total number of active recipients in provincial program); UC=universal coverage; Vet=veterinarian; wk=week; yr=year; *=plus 2 non-voting.*

Table 14. Canadian Provincial External Advisory Committees (EAC)--Activities

Prov	*UC*	*EAC*	*Mandates*	*Clin/Econ Eval*	*Timeline*	*Fast*	*Vol (95/96)*	*Monitor*	*Effect*	*External*	*Finance*	*Overall*
ON	√	DQTC (Drug Quality and Therapeutics Committee)	safety, efficacy, alternatives, cost-benefit, c-e monitor use educate/liason	CLIN: 'Clinical Data Checklist'--safety, efficacy, comparisons ECON: pharmacoeconomic analysis/worksheet; financial impact analysis (ON Guidelines)	2-4 mos	yes	new: 393 list: 269			advise MOH, ODB	1996: $1.3 B	
BC	√	TI=Therapeutics Initiative (DAWG=Drug Assessment Working Group, subset of TI)	review/disseminate best therapeutic info to professions & Pharmacare	CLIN: syst. review re safety & efficacy; int/ext review.	ss: sev mos ms: few wks	no				DAWG presents to TI; TI to PI, Pharmacare DBC	1996: $271M	
		PI=Pharmacoeconomic Initiative	c-e analysis advising Pharmacare re c-e formulary	CLIN-ECON: builds on TI review, adds c-e assessment per ON guidelines				impact analysis (financial, utilization, subs), pro/retro		PI f/u to TI, then submits to DBC	MOH&MRS budget: 98/99-$250K	*low manufacturer compliance with economic guidelines*
AB		EC&DC=Expert Committee & Drug Approval	advises MOH&W re new & current drugs on formulary scientific, therapeutic, clinical, socio-economic eval	CLIN: clinical studies demonstrating safety/effectiveness, ther advantages ECON: ON Guidelines	3-4 mos	yes				part of Alberta Blue Cross reports to minister	95/6: $154M	
SK	√	DQAC=Drug Quality Assessment Committee	eval new drug submissions	CLIN: therapeutic value, advantages; lit review (no cost eval'n)	3-4 mos	yes	evaluates 200-300/yr (1998)			reports to SFC	Max Allowable Cost (within interchangeable groups) Standing Offer Contract (SOC)—saved $10M in 99/00	
		SFC=Saskatchewan Formulary Committee	c-e for new or current drugs advises re formulary	CLIN-ECON: f/u from DQAC assessment, cost-impact; possibly use ON guidelines for hi-cost						sets formulary subject to ministerial approval		*'not constrained by budgetary ceiling' (considers merits and value for money)*
MB	√	MDSTC=Manitoba Drug Standards and Therapeutics Committee	assess therapeutic & economic value of new drugs formulary rec's	CLIN: therapeutic value, alternatives, interchange ECON: cost-impact on pharmacare budget	ss: 3 mos ms: 2 mos	no	new: 270 list: 260 (1995)			reports to MOH	95/6: $78M	

APPENDIX II. CANADIAN: TABLES & FIGURES

Prov	*UC*	*EAC*	*Mandates*	*Clin/Econ Eval*	*Timeline*	*Fast*	*Vol (95/96)*	*Monitor*	*Effect*	*External*	*Finance*	*Overall*
QC	√	CCP= Conseil Consultatif de Pharmacologie	advise minister re therap value & drug pricing	CLIN/ECON: ?			rev'd: 335 list: 260			advises MOH&SS	1994: $733M	*2001-2 plan to integrate CCP, CRUM & RRM (a hospital drug utilization review committee)*
		CRUM=Comité de Revue de l'Utilisation des Médicaments	review & improve use of medicines	CLIN/ECON: consider expected results, efficiency, efficacy, economic/health impacts						as above works w CCP & other grps		
NB		PDPAUC=Prescription Drug Program Advisory and Utilization Committee	evaluate, recommend formulary changes monitor use	CLIN/ECON: ?	ss: 2-6 mos ms: 3-4 mos	no				advises MOH&CS	96/7: $53M	
NS		D&TC=Drug and Therapeutics Committee	evaluate new drugs, interchangeability	CLIN/ECON: internal/external review	3-6 mos	no				advise FMC	95/6: $90M	
		FMC=Formulary Management Committee	recommend to MOH drug benefits to Pharmacare programs	CLIN/ECON: must demonstrate therap or economic adv all new ss drugs ext. rev.						advise MOH		
PE		PAC=Pharmacy Advisory Committee	recommend to MOH re develop & regular review of all drug programs	same criteria as SK formulary submissions	>2yrs (as of July 98, due to freeze, backlog)	no	new: 105 list: 0 (frozen)			advise MOH	95/6: $7M	
		PBC=Pharmacy Board Committee	interchangeable drug list	interchangeable lists merged with NS; inclusion criteria same as NS and SK						advise Lt Gov in Council		
NF		NLPDP (formerly NIDPFC)=Newfoundland & Labrador Prescription Drug Program	evaluate new drugs, recommend formulary changes; interchangeability	CLIN: safety/efficacy studies ECON: ON Guidelines; cost-benefit analysis internal review: if not clear then Ad Hoc committee (possible involvement w Atlantic Drug Programs Joint Review Committee)	2-6 mos	informal				advise MOH	95/6: $39M	

Table 15: Provincial Government Drug Spending 1990-1997
(in millions Of $US) (from Menon, 2001)

Province	1990	1997	% change
British Columbia	$154.4	$257.0	+67
Alberta	120.9	171.1	+42
Saskatchewan	58.7	43.2	-27
Manitoba	32.7	54.7	+67
Ontario	589.9	871.5	+48
Nova Scotia	55.8	60.5	+8
Total	1,012.3	1,458.0	+44

Note: Includes ingredient costs, markups, and dispensing fees.
Source: Federal/Provincial/Territorial Task Force on Pharmaceutical Prices.

APPENDIX III. ODB/DQTC RESOURCES

Table 16. Clinical Data Checklist

***Product Name/Manufacturer*:** _____

Drug Product	***Page Ref(s)***
1. What is the pharmacological mechanism of the drug?	
2. What are the drug's Health Canada approved indications?	
3. What is the recommended dose range and duration of therapy? (Please include relevant patient populations - e.g., the elderly)	
4. What Formulary/CDI listing status is proposed by the manufacturer?	
Clinical Evidence	
1. What are the conclusions of randomized controlled trials supporting the efficacy (i.e. when used under optimal circumstances) of the product? Are trials published in peer-reviewed journals?	
2. What are the key comparators for this drug product? Which ones are listed in the Formulary/CDI?	
3. What are the results of randomized trials comparing the product to listed alternatives on the Formulary/CDI? Are there randomized trials comparing the product to the least costly and most widely used alternative products listed in the Formulary/CDI?	
4. What are the conclusions of randomized controlled trials supporting the effectiveness (i.e., when used under usual, real world circumstances) of the product? Are trials published in peer-reviewed journals?	
5. Do the randomized trials use the most clinically relevant outcome measures, or do they use the surrogate outcomes requiring extrapolation to the relevant outcome? Are the end-point(s) sufficiently justified?	
6. Were any clinical studies conducted in the elderly, women and children? If not, why not?	
7. Were any of the clinical trials conducted in Canada?	
8. Are there ongoing trials that would provide additional information on the product?	
9. What are the contraindications for the product?	
10. What are the side effects of the drug product?	
11. Are there particular safety issues of concern to recipients of the ODB program (e.g., safety in the elderly, women and children)?	
12. If the product contains a combination of drugs, is there a pharmacologic and pharmacokinetic rationale for the combination? Specifically, does each component of the combination make a contribution to the claimed effect(s)? Is the dose of each component appropriate for the elderly and/or children? Is the effect of either component modified (synergistically or antagonistically) by the addition of the other component?	

Table 16 (cont)

Drug Utilization	*Page Ref(s)*
1. What are the Health Canada approved patient population group(s) for the drug?	
2. Will clinicians be able to easily and precisely determine which patients should be treated with this drug? Please explain.	
3. Are there other clinical uses or trials for non-approved Health Canada indications?	
4. Is it likely that clinicians will expand the use of the product for conditions not approved by Health Canada? If not, what is the evidence to support this position?	
5. What is the projected number of patients in Ontario covered by ODB who will use the product in a year?	
6. Are there utilization data for the drug product in other jurisdictions? If so, please discuss the possible utilization impact for ODB.	

APPENDIX III. ODB/DQTC RESOURCES

Table 17. Pharmacoeconomic Analysis Summary

SECTION I. DRUG PRODUCT

Product Information	
Brand Name / Manufacturer	*Drug X Tablet USP (ACME Ltd.)*
Generic Name / Strength / Dosage Form	*Generic C 5 mg Tablet*
DIN	*01234567*
Usual Dose Regimen/Duration	*5 mg bid x 10 days*
Submitted Price Per Unit	*$2.00 per tab*
Daily Cost *	*$ 4.00 per day*

* based on usual dosing regimen and submitted price, as stated above

Available Package Size (A)	Price (B)	Calculated Price/Unit (C = B/A)	Cost of Usual Dosing Regimen
50	*$ 100.00*	*$ 2.00 per tablet*	*$ 40.00*
100	*$200.00*	*$ 2.00 per tablet*	*$ 40.00*
500	*$ 1000.00*	*$ 2.00 per tablet*	*$ 40.00*

SECTION II. COMPARATOR DRUG PRODUCT / TREATMENT

Please indicate all appropriate drug comparators (including strength and dosage form) and/or treatment comparators for this product.

Generic Name (Mfr) / Strength / Dosage Form	Price *	Equivalent Dosing Regimen for Comparator	Daily Cost	Cost of Usual Dosing Regimen
Generic A (Brand Y Inc) 5 mg USP tab	*$1.00*	*5 mg bid x 10 days*	*$2.00*	*$20.00*
Generic B (Brand Z Inc) 5 mg BP cap	*$1.50*	*5 mg tid x 7 days*	*$4.50*	*$31.50*

* indicate source if other than the price in the Formulary/CDI.

Table 17 (cont)

SECTION III. COMPARATIVE OUTCOMES

Drug	Outcome 1 (e.g. successes)	Outcome 2 (e.g. adverse events)	Outcome 3 (e.g. deaths)	Outcome 4 (e.g. projected survival)
Drug X	***$ 70%***	***5%***	***1%***	***20 years***
Generic A	*$ 80%*	*10%*	*2%*	*18 years*
Generic B	*$ 70%*	*10%*	*3%*	*16 years*

References:

Note:

- Appropriate comparators should be listed for each strength and dosage form.
- The manufacturer should indicate comparable dosing regimens, including the duration of therapy.
- Where there are multiple source alternatives for the products, the lowest cost interchangeable alternatives should be listed first.
- Where there are listed single source alternatives for the product, these may also be listed.
- Where there are no appropriate listed single or multiple source alternatives, other marketed drug products may be listed.
- Where the appropriate comparison is not a drug but another treatment, please attach a separate sheet outlining the treatment and indicating why it is the appropriate comparator.

SECTION IV. PHARMACOECONOMIC ANALYSIS

Pharmacoeconomic Analysis included? [ ] Yes [ ] No

Pharmacoeconomic Worksheet included? [ ] Yes [ ] No

If yes, please indicate type of analysis:
[ ] Cost-Minimization
[ ] Cost-Consequence
[ ] Cost-Effectiveness
[ ] Cost-Utility
[ ] Cost-Benefit

If a detailed economic analysis is **not** included, please outline the reasons below:

Table 18. Pharmacoeconomic Analysis Work Sheet

Product Information	
Drug Product (generic name/strength/dosage form)	*Drug X Tablet USP* *Generic C 5 mg Tablet*
Name of Manufacturer	*ACME Ltd.*

Please complete each of the following questions:

1. (a) What is the question being asked in the analysis?
   (b) What type of economic analysis was performed to answer the question?
      i Cost comparison
      ii. Cost-consequence analysis
      iii. Cost-effectiveness analysis
      iv. Cost-utility analysis
      v. Cost-benefit analysis
   (c) What is the justification for the approach taken?

2. (a) Did the study involve a comparison of alternative treatments for patients with the same clinical condition?
   (b) Are those alternatives explicitly stated?
   (c) Is the analysis therefore an incremental analysis?

3. (a) Is the viewpoint or perspective for the analysis stated clearly?
   (b) Is it a societal perspective, third-party payer perspective, patient perspective?
   (c) Is the analysis presented in a disaggregated fashion showing these perspectives separately?

4. (a) Was the evidence of the product's efficacy established through randomized trials?
   (b) Was this evidence of efficacy supplemented by evidence of effectiveness applicable to the patients covered by the Ontario Drug Benefit program?
   (c) Was the latter evidence derived from studies documenting routine use in clinical practice?

5. (a) Are the methods and analysis displayed in a clear and transparent manner?
   (b) Are the components of the numerator (cost of each alternative) and denominator (clinical outcomes of each alternative) displayed?
   (c) Are clinical outcomes expressed first in natural units and then translated into alternative units such as benefits or utility? (See Section 3.4.d. of the *Ontario Guidelines for Economic Analysis of Pharmaceutical Products* for suggested format).

Table 18 (cont)

6. Are all important and relevant costs and consequences (outcomes), including adverse effects, for each alternative identified?

7. (a) Are costs and consequences modelled as in a decision tree with information derived from a variety of sources; OR
   (b) estimated directly from a variety of sources; OR
   (c) estimated directly from a specific patient population?

8. (a) Are capital costs and overhead costs included as well as operating costs?
   (b) How were they measured?

9. How were indirect costs identified and estimated?

10. How was quality of life measured?

11. (a) What equity assumptions were made in the analysis?
   (b) For example, are QALYs gained by any individual considered equal?

12. (a) If some variables were difficult to measure, how did the authors handle this difficulty?
   (b) Did they slant the analysis all in favour of one intervention in order to bias the analysis against the desired result?

13. (a) Were extensive sensitivity analyses performed?
   (b) What were the ranges of values for variables in the sensitivity analyses?

14. (a) Is quality of life an important component of an economic analysis of this question?
   (b) How sensitive is the estimate of cost utility to variations in quality of life?

15. (a) Is there an estimate of the aggregate incremental expenditure required for the province to provide this product to patients covered by its programs?
   (b) What is the estimate of aggregate incremental costs?
   (c) Does this estimate cover all of the major indications for use of the product?

16. (a) Has the incremental cost-effectiveness ratio been estimated for a special clinical indication that represents the majority or all of its expected use by those covered under the Ontario Drug Benefit program?
   (b) Do these other indications involve a large amount of utilization for which the ratio may be very different?

Table 18 (cont)

17. (a) Who performed the analysis?

    (b) Did the authors of the report sign a letter indicating their agreement with the entire document presented?

    (c) Does the report indicate that the authors had independent control over the methods and right to publish the analysis regardless of its results?

18. What is the "bottom line" result of the analysis in quantitative terms? The answer to this question will be statements like the following:

    - The cost per QALYs gained for using this product compared to the alternative is $X, or ranges from $Y to $Z.
    - The use of this product compared to the stated alternative will result in an expected incremental expenditure of $X per patient treated with a net reduction of Y major adverse clinical events (e.g., cardiac deaths) and Z minor clinical events (e.g., side effects).

APPENDIX III. ODB/DQTC RESOURCES

Table 19. ODB Financial Impact Analysis Summary

SECTION I. DRUG PRODUCT

Product Information	
Drug Name / Manufacturer	
Generic Name / Strength / Dosage Form	
Proposed reimbursement status	
DIN	
Submitted Price Per Unit	
Daily Cost *	
Usual Dosing Regimen/Duration	
Maximum Dosing Regimen/Duration	

* based on usual dosing regimen and submitted price, as stated above.

SECTION II. SUMMARY OF ODB FINANCIAL IMPACT

Summary Item	Manufacturer's Submitted Estimates		
	Year 1	Year 2	Year 3
Drug Cost* ($)			
Claims			
Net Expenditure/(Savings)			

* Drug Cost should exclude up-charge and professional fee.

Table 19 (cont)

SECTION III: UNDERLYING ASSUMPTIONS FOR KEY FACTORS IN FORECAST – MOST LIKELY SCENARIO

For each parameter, it would be helpful to organize the data according to Baseline (where applicable), Year 1, Year 2, and Year 3 with the confidence level (high, medium or low) and the evidence/data sources.

Parameter	Baseline	Year 1	Year 2	Year 3	Confidence Level (high/med/low)	Evidence used to support assumptions
1. Disease Demographics (e.g. number of patients with the disease, number of patients consulting physicians, number of patients diagnosed, number of patients treated, number of ODB recipients)						
2. Market Share For (1) submitted product; (2) comparators within therapeutic class; (3) other relevant comparators for therapeutic indication.						
a) Patients (e.g. new patients, patients switching from competitor products)						
b) Claims (e.g. claims/ patient, claims/year)						
3. Growth Rate (e.g., compliance rate, withdrawal rate, potential impact of future listings such as new generic products)						
4. ODB Expenditures For (1) submitted product; (2) comparators within therapeutic class; (3) other relevant comparators for therapeutic indication.						
a) Cost per claim (e.g. doses per day, cost per dose, cost per day)						
b) ODB claims per year						
c) Total expenditures						
d) Net impact						

Table 19 (cont)

SECTION IV. CONTINGENCY ESTIMATES – PESSIMISTIC AND OPTIMISTIC SCENARIOS

For each parameter, it would be helpful to organize the data according to Baseline (where applicable), Year 1, Year 2, and Year 3 with the confidence level (high, medium or low) and the evidence/data sources.

Parameter	Baseline	Year 1	Year 2	Year 3	Confidence Level (high/med/low)	Evidence used to support assumptions
PESSIMISTIC SCENARIO (SUBMITTED PRODUCT PERFORMANCE IS BELOW EXPECTATIONS)						
Total annual ODB expenditure (submitted product) ($)						
Incremental change vs. most likely forecast ($)						
Total ODB expenditure (therapeutic class) ($)						
Incremental change vs. most likely forecast ($)						
Rationale for changes (list/identify any significant modifications in assumptions)						
OPTIMISTIC SCENARIO (SUBMITTED PRODUCT PERFORMANCE EXCEEDS EXPECTATIONS)						
Total annual ODB expenditure (submitted product) ($)						
Incremental change vs. most likely forecast ($)						
Total ODB expenditure therapeutic class) ($)						
Incremental change vs. most likely forecast ($)						
Rationale for changes (list/identify any significant modifications in assumptions)						

APPENDIX IV. CANADA HEALTH ACT, SDP AND CCO RESOURCES

Funding For In-Hospital Drug Therapies In Ontario Public Hospitals

Relevant Statutes and Regulations

Several sections of the Ontario Health Insurance Act, R.S.O. 1990 (the Health Insurance Act) [91;92] and the Public Hospitals Act [93-95] are relevant to the funding of medications administered to insured persons while in an Ontario public hospital. Important sub-sections follow. For the purposes of the Act, "in-patients" are persons admitted to and assigned a bed in a hospital in-patient area, and "out-patients" are those who receive out-patient services and are not admitted to an in-patient area.

Health Insurance Act – Regulation 552 (Amended to O. Reg. 322/01)

Insured Hospital Services in Canada

Section 7: In-patient Services

Subject to section 10, the in-patient services to which an insured person is entitled without charge are all of the following services:
Paragraph 4 (of 5)
Drugs, biologicals and related preparations that are prescribed by an attending physician or midwife in accordance with accepted practice and administered in a hospital, but not including any proprietary medicine as defined from time to time by the regulations made under the *Food and Drugs Act* (Canada). (R.R.O. 1990, Reg. 552, s. 7; O. Reg. 794/93, s. 2.)

Section 8: Out-patient Services

The out-patient services to which an insured person is entitled without charge are all of the following services:

1. Laboratory, radiological and other diagnostic procedures, together with the necessary interpretations.
2. The use of radiotherapy, occupational therapy and physiotherapy facilities where available in a hospital in Canada when prescribed by a physician.
3. The use of speech therapy facilities where available in a hospital in Canada when prescribed by a physician.
4. The use of diet counselling services when prescribed by a physician.
5. The hospital component of all other out-patient services, including the use of an operating room and anesthetic facilities, surgical supplies, necessary nursing service, meals required during a treatment program and the supplying of drugs, biologicals and related preparations that are prescribed in accordance with accepted practice by a physician on the medical staff or a midwife on the midwifery staff of the hospital and that are administered in the hospital, but not including:

a) the provision of any proprietary medicine as defined from time to time by the regulations made under the *Food and Drugs Act* (Canada),

b) the provisions of medications for the patient to take home, diagnostic services performed to satisfy the requirements of third parties such as employers and insurance companies, and
c) visits solely for the administration of drugs, vaccines, sera or biological products. (R.R.O. 1990, Reg. 552, s. 8; O. Reg. 794/93, s. 3; O. Reg. 175/95, s. 1 (1, 2).)

Exception 1

Despite subparagraph (b) of paragraph 5, the provision of a medication listed in Column 1 of the Table [Appendix I] to this subsection to an out-patient, for use in the home, is an out-patient service to which an insured person is entitled without charge if the medication is provided in the circumstances described in Column 2 of the Table [Appendix I]: (O. Reg. 175/95, s. 1 (3); O. Reg. 253/00, s. 1; O. Reg. 322/01, s. 1.)

Exception 2

Despite subparagraph (d) of paragraph 5, the following visits to a hospital are out-patient services to which an insured person is entitled without charge:
a) A visit that is solely for the administration of a rabies vaccine.
b) A visit that is solely for the administration of a medication listed in Column 1 of the Table [Appendix I]to subsection (2) if the conditions listed in Column 2 of the Table [Appendix 1] are satisfied. O. Reg. 175/95, s. 1 (3).

Section 9: Hospitals Eligible for the Provision of Insured Services

Subject to section 10 and subsection 11 (1), an insured person is entitled to in-patient services and out-patient services in the following hospitals, without paying any charge to the hospital for such services:
1. A hospital listed in Schedule 2.
2. A hospital graded, under the *Public Hospitals Act*, as a Group A, B, C, E, F, G, J or R hospital. (O. Reg. 253/00, s. 2 (1); O. Reg. 322/01, s. 2 (1).)

Section 10: Co-payment

10. (1) A co-payment for accommodation and meals that are insured services shall be made by or on behalf of an insured person who, in the opinion of the attending physician, requires chronic care and is more or less permanently resident in a hospital or other institution. O. Reg. 496/96, s. 3.

Section 11 (1): Patients Eligible to Receive Insured Hospital Services

11. (1) An insured person is not entitled to insured services in a hospital unless the person has been,
a) admitted as an in-patient on the order of a legally qualified medical practitioner;
b) received in the hospital and examined as an out-patient by a legally qualified medical practitioner and treated as an out-patient, if necessary;
c) referred to the hospital as an out-patient by,
   (i) a physician, for any of the services designated in section 8, or

(ii) an osteopath or chiropractor, for X-rays;

d) admitted as an in-patient or registered as an out-patient on the order or under the authority of a midwife; or

e) registered as an out-patient, solely for the purpose of undergoing a diagnostic procedure, on the order or under the authority of a registered nurse in the extended class. (R.R.O. 1990, Reg. 552, s. 11 (1); O. Reg. 794/93, s. 5; O. Reg. 44/98, s. 3.)

Section 28: Payment by contribution to annual expenditures

Any amounts payable to or on behalf of an insured person under the [Ontario Health Insurance] Plan in respect of insured services provided by or in a hospital or health facility may be paid in the form of the payment by the Province of all or any part of the annual expenditures of such hospital or health facility, where such payment by the Province is authorized under any Act. (R.S.O. 1990, c. H.6, s. 28.)

Public Hospitals Act - R.S.O. 1990, c. H.40, s. 5.

Payments to hospitals

5. (1) The Minister [Ontario Minister of Health and Long-term Care] may pay any grant, make any loan and provide any financial assistance to a hospital if the Minister considers it in the public interest to do so.

In sum, with the exception of drugs listed under Section 8, Regulation 552 of the Health Insurance Act and I.V. therapies covered under a special funding arrangement established by Cancer Care Ontario (see below), medications administered to in-patients in Ontario public hospitals must be paid for through the hospital's global budget. According to Section 8, Regulation 552 of the Act, out-patient services to which an insured person is entitled without charge exclude nursing care, surgical supplies, prescribed medicines, and other goods and services that are normally associated with out-patient treatment programs if a patient's visit is solely for the administration of drugs, vaccines, sera, or biological products.

Table 20. Canada Health Insurance Act
--Regulation 552 (Amended To O. Reg. 322/01) Insured Hospital Services In Canada - Section 8 (Exceptions 1 And 2): Out-Patient Services

ITEM	COLUMN 1 *Medication Provided*	COLUMN 2 *Condition of Insured Service*
1.	A medication for the emergency treatment of, or the prevention of, a hemorrhage	1. The medication must be available in a hospital in Ontario. 2. The medication must be prescribed by a physician on the medical staff of that hospital. 3. The medication must be provided to a patient with haemophilia.
2.	Cyclosporine	1. The medication must be prescribed by a physician on the medical staff of a hospital graded, under the *Public Hospitals Act*, as a Group O hospital. 2. The medication must be provided to a solid organ or bone marrow transplant patient.
3.	Zidovudine, commonly called "AZT"	1. The medication must be prescribed by a physician. 2. The medication must be provided to a patient with HIV infection.
4.	A biosynthetic human growth hormone	1. The medication must be prescribed by a physician on the medical staff of a hospital graded, under the *Public Hospitals Act*, as a Group S hospital. 2. The medication must be provided to a patient with endogenous growth hormone deficiency.
5.	A medication for treatment of cystic fibrosis that is listed in Schedule 17	1. The medication must be prescribed by a physician on the medical staff of a hospital graded, under the *Public Hospitals Act*, as a Group T hospital.
6.	A medication for the treatment of thalassemia that is listed in Schedule 18	1. The medication must be prescribed by a physician on the medical staff of a hospital graded, under the *Public Hospitals Act*, as a Group U hospital.
7.	Erythropoietin	1. The medication must be prescribed by a physician on the medical staff of a hospital. 2. The medication must be provided to a patient with anaemia of end-stage renal disease.
8.	Alglucerase	1. The medication must be prescribed by a physician. 2. The use of the medication must be recommended by the Gaucher's Disease Review Committee. 3. The medication must be provided to a patient with Gaucher's disease.

ITEM	COLUMN 1 *Medication Provided*	COLUMN 2 *Condition of Insured Service*
9.	Clozapine	1. The medication must be prescribed by a physician on the medical staff of a hospital. 2. The use of the medication must be recommended by a regional co-coordinator of a provincial psychiatric hospital. 3. The medication must be provided to a patient with treatment-resistant schizophrenia.
10.	Diagnosing, commonly called "ddI"	1. The medication must be prescribed by a physician. 2. The medication must be provided to a patient with HIV infection.
11.	Zalcitabine, commonly called "ddC"	1. The medication must be prescribed by a physician. 2. The medication must be provided to a patient with HIV infection.
12.	Pentamidine	1. The medication must be prescribed by a physician. 2. The medication must be provided to a patient with HIV infection.

(O. Reg. 175/95, s. 1 (3); O. Reg. 253/00, s. 1; O. Reg. 322/01, s. 1.)

Table 21. Public Hospitals Act
-- Regulation 964 (Amended to O. Reg. 321/01): Classification of Hospitals

1. (1) Hospitals are classified as general hospitals, convalescent hospitals, hospitals for chronic patients, active treatment teaching psychiatric hospitals, active treatment hospitals for alcoholism and drug addiction and regional rehabilitation hospitals, and are graded as,

a) Group A hospitals, being general hospitals providing facilities for giving instruction to medical students of any university, as evidenced by a written agreement between the hospital and the university with which it is affiliated, and hospitals approved in writing by the Royal College of Physicians and Surgeons for providing post-graduate education leading to certification or a fellowship in one or more of the specialties recognized by the Royal College of Physicians and Surgeons;
b) Group B hospitals, being general hospitals having not fewer than 100 beds;
c) Group C hospitals, being general hospitals having fewer than 100 beds;
d) Group D hospitals, being hospitals that treat patients suffering from cancer, that undertake research with respect to the causes and treatment of cancer and that provide facilities for the instruction of medical students;
e) Group E hospitals, being general rehabilitation hospitals;
f) Group F hospitals, being hospitals for chronic patients having not fewer than 200 beds but not including Group R hospitals;
g) Group G hospitals, being hospitals for chronic patients having fewer than 200 beds but not including Group R hospitals;
h) Group H hospitals, being psychiatric hospitals providing facilities for giving instruction to medical students of any university;
i) Group I hospitals, being hospitals for the treatment of patients suffering from alcoholism and drug addiction;
j) Group J hospitals, being hospitals designated by the Minister to provide special rehabilitation services for disabled persons in a region of Ontario specified by the Minister for each hospital;
k) Group K hospitals, being separate organized facilities approved as such by the Minister, to provide local diagnostic and treatment services in a community or district to handicapped or disabled individuals requiring restorative and adjustive services in an integrated and co-ordinated program;
l) Group L hospitals, being hospitals for the treatment of patients suffering from alcoholism and drug addiction and providing facilities for giving instruction to medical students of any university as evidenced by a written agreement between the hospital and the university with which it is affiliated;
m) Group M hospitals, being hospitals that may charge and accept payment from other hospitals for the performance of computerized axial tomography scans;
n) Group N hospitals, being hospitals that may acquire and operate magnetic resonance imaging equipment and may charge and accept payment from other hospitals for the performance of magnetic resonance imaging;
o) Group O hospitals, being hospitals used as transplantation centres;
p) Group P hospitals, being hospitals that may acquire and operate extra corporeal shock wave lithotripsy equipment;
q) Group Q hospitals, being hospitals that may provide in vitro fertilization services;

r) Group R hospitals, being facilities for chronic patients that are called continuing care centres;
s) Group S hospitals, being hospitals that provide biosynthetic human growth hormones;
t) Group T hospitals, being hospitals that may act as distributing centres for drugs for cystic fibrosis treatment and that provide drug-related therapy for cystic fibrosis treatment;
u) Group U hospitals, being hospitals that may act as distributing centres for drugs for thalassemia treatment and that provide drug-related therapy for thalassemia treatment; and
v) Group V hospitals, being hospitals that operate ambulatory care centres.
(R.R.O. 1990, Reg. 964, s. 1 (1); O. Reg. 172/95, s. 1; O. Reg. 611/98, s. 1; O. Reg. 321/01, s. 1.)

2. The hospitals, their classifications and grades are set out in the list maintained by the Minister under subsection 32.1 (2) of the Act and available on the Internet, through the website of the Ministry of Health and Long-Term Care at http://www.gov.on.ca/health. (O. Reg. 251/00, s. 1.)

Independent Legal Interpretation of the Canadian Health Insurance Act

by Mary Jane Dykeman, Barrister & Solicitor

"Many elements of the health care system (e.g., drugs, long term care) are not covered under [the Canada Health Act] which results in hospitals being pressured to provide services to patients who might otherwise be treated outside the system."

University Health Network submission
to the Romanow Commission, September 26, 2001[1]

Question

You have requested a review of the question of funding for drug therapies in Ontario hospitals. Specifically, ICES has been solicited by the Ontario Council of Teaching Hospitals to examine the issue of how to manage costly medications in the hospital environment. Significant concerns have been raised about a hospital's responsibility to provide drug coverage to out-patients.

You have stated that some hospitals believe that the provincial government should be responsible for covering these costs, and the government's position is that hospitals continue to be responsible for this coverage (presumably, pursuant to the HIA, to be paid out of the hospitals' global budgets). An interpretation of the *Health Insurance Act* [2] is required with respect to medications administered to in- and out-patients in public hospitals, with a view to determining who should pay for these medications.

Answer

Do teaching hospitals have the right to unilaterally force the provincial government to assume funding for specific out-patient drug coverage? In my view, they do not. May hospitals refuse to pay for drugs administered to their in-patients? Under the HIA, they may do so only if the out-patient's visit is solely for the purpose of administering the drug, unless the out-patient falls under the exceptions listed in the HIA (in those prescribed instances, the provincial government will provide coverage). Subject to the exceptions, where the visit is solely for the purpose of administering the drugs, it would appear that the out-patient or their health insurer must pay for the drugs received. If the visit is not solely for the administration of the drug (e.g., provided during day surgery in an out-patient clinic), the hospital must bear the associated costs.

In Canada, responsibility for health care rests primarily with provincial and territorial governments. The federal government's main control over health services exists through the

[1] "A Presentation From the University Health Network to the Commission on the Future of Health Care in Canada", September 26, 2001, at p. 14, *sub. nom.* "Romanow Commission". Available on-line at: http://www.uhn.ca, under "What's New" (accessed November 17, 2001).
[2] R.S.O. 1990, c. H.6 [hereinafter "HIA"].

Canada Health Act.[3] As a condition of full federal funding, provinces are required to provide health services in accordance with a number of criteria (discussed more fully in the Analysis section of this opinion). Once federal funding is received by provincial governments, payments have traditionally been made to public hospitals and other health facilities, which pay for these services through their global budgets.

In Ontario, there is sufficient legislative authority under the HIA for the provincial government to make decisions about which services to insure or not, and to limit coverage for drug therapies to those administered in hospital. There are exceptions to this general rule:

- statutory exceptions (as set out in the regulations to the HIA);
- drugs covered through a provincial government program (the Special Drugs Program);
- drugs covered by way of agreement (as is the case with the New Drug Funding Program administered by Cancer Care Ontario).

The utilization of drug therapies is escalating, yet the high costs of many new drugs prescribed in teaching hospitals form part of the specialized services offered. There are a number of options to consider in moving toward a resolution of this problem:

Status quo: Hospitals may continue to cover drugs provided to in-patients where they are required as part of the service being provided, e.g. day surgery. They are not required to provide coverage for drugs administered to in-patients, where the purpose of the hospital visit is solely for the administration of the drug, unless the drugs fall under one of the exceptions to the general rule set out in the HIA. In that case, the provincial government provides coverage through its Special Drugs Program.

I have not been privy to the existence of any binding funding contracts between the government and the teaching hospitals, and as such, am assuming that no such contracts exist. If they do, they will be the first source of information as to the funding arrangements agreed to.

An option for the teaching hospitals, which has undoubtedly already been undertaken in a variety of ways, may be to lobby at the provincial level with the goal of entering into agreements for the funding of specific drug therapies. (However, your written comments to me regarding the provincial audit of the MOHLTC Special Drugs Program, its recommendation against an expansion of the program, and the potential for its demise, lead me to conclude that while important to preserving a relationship with the provincial government, the odds of success of such lobbying efforts in the longer term are questionable.)

Submissions to groups such as the Romanow commission at the national level, as undertaken by the University Health Network, also secure a legacy of participation in the public policy debate. At both the provincial and federal levels, this type of work is critical, as teaching hospitals will demonstrate their role as partners in a shared system. It may also result in increased public support for the teaching hospitals should the latter adopt the 'cause' of those who argue the denial of out-patient drug coverage constitutes a breach of their Charter-protected rights.

[3] R.S.C. 1985, c. C-6 [hereinafter "CHA"].

Caselaw on the ability to challenge government policy decisions is quite unequivocal, and suggests that the teaching hospitals would not necessarily be successful in challenging the decision not to fund further out-patient drug coverage on the basis of tort law.

On the authority of the Supreme Court of Canada in *Just v. British Columbia*[4] and other similar cases, it is clear that pure policy decisions made by a public authority such as a government department should not be subject to review by the courts. The actions taken by government must have appropriate statutory authority, which they do in this case through the HIA and PHA. As well, it would have to be shown that the decision-maker (likely the Minister or his or her delegate) improperly exercised the discretion to provide drug coverage. With respect to what constitutes a policy decision, the courts have stated that the government does not owe a duty of care (nor will it be found liable for a tort of negligence) where a decision is made within the proper scope of its legislative authority, as "dictated by financial, economic, social or political factors or constraints".[5] In the context of drug coverage, a party would have to prove that the government owed a duty of care, breached that duty, and that any resulting harm could be linked to the government's action or inaction. Given the many competing arguments for use of scarce resources that could be put forward, this is difficult to achieve, particularly where the parameter for the exercise of ministerial discretion is "the public interest".

The reasoning in a more recent Supreme Court of Canada case may merit further attention: *Eldridge v. British Columbia (Attorney General)*.[6] In that case, the court held that to the extent that they are charged with implementing government policies, public hospitals are subject to the *Canadian Charter of Rights and Freedoms.*[7] On that basis, the teaching hospitals could consider taking the position that the failure to fund certain out-patient drug therapies constitutes an infringement of the individual's s. 15(1) right to equality. The caveat is that a Charter challenge must emanate from the allegedly affected individual, and not from the hospitals.

The Special Drugs Program (SDP) of MOHLTC now covers a limited number of drugs for specific conditions and in specific circumstances. By way of example, a person suffering from a serious mental disorder could query why clozapine is funded through SDP, while another drug is not. Strategically, a teaching hospital should carefully consider whether to force expanded drug coverage on the basis of *Eldridge.* The risk is that it could create a 'floodgates' effect: a court could find that a Charter breach had occurred, the government could agree, but still require hospitals to make decisions about funding through provision of services via their global budget process.

[4] [1989], 2 S.C.R. 1228.
[5] *Brown v. British Columbia (Minister of Highways and Transportation)* [1994], 1 S.C.R. 420 at para. 27 (Q.L.), quoting *Just v.British Columbia* [1989], 2 S.C.R. 1228.
[6] [1997], 3 S.C.R. 624 (S.C.C.).
[7] Part I of the *Constitution Act,* being Schedule B to the *Canada Act 1982* (U.K.), c. 11 [hereinafter "Charter"].

APPENDIX IV. CANADA HEALTH ACT, SDP AND CCO RESOURCES

Background

1. Provincial Responsibility for Health Care

In Canada, responsibility for provision of health care arises out of the constitutional division of powers between the federal and provincial governments. As one legal scholar notes:

> It seems, however, to be generally agreed that provinces have exclusive jurisdiction over insurance for and supply of health goods and services pursuant to ss. 92(7) (hospitals), 92(13) (property and civil rights) and 92(16) (matters of a merely local or private nature) of the *Constitution Act, 1867*.[8]

This provincial jurisdiction over health, and specifically hospitals, was reiterated in the 1997 Supreme Court of Canada decision in *Eldridge*:[9]

In order to receive a full cash contribution from the federal government for the FY, each province must deliver "medically necessary" services in accordance with the five tenets of the *Canada Health Act*:[10]

1. comprehensiveness
2. accessibility
3. universality
4. portability
5. administration[11]

It is generally the case that hospitals receive funding from the applicable provincial or territorial government, and pay for these services out of their global budgets. This is the norm in Ontario, and in British Columbia, as was acknowledged by the Supreme Court in *Eldridge*:

Hospitals in British Columbia are funded through lump sum "global" payments that they are for the most part free to allocate as they see fit. They are rarely ordered by government to provide specific services. In those instances, they are generally required to fund the service out of their global budgets. The government does provide some funding for specific programs, such as heart transplantation, but this is infrequent. [12]

---

[8] C. Flood, "The Structure and Dynamics of Canada's Health Care System" in *Canadian Health Law and Policy*, J. Downie and T. Caulfield, eds. (Toronto: Butterworths, 1998), relying on *Eldridge v. British Columbia (Attorney General)*, *supra*, note 6 at para. 24.
[9] *Supra,* note 6 at para. 24 (Q.L.).
[10] CHA, s. 5.
[11] CHA, s. 7; for a full explanation of these criteria, see ss. 8-12 [CHA].
[12] *Supra*, note 6 at para 10 (Q.L.).

2. Health Insurance Act

The primary function of the HIA is to create a health insurance scheme to which all residents of Ontario are entitled.[13] The Ontario Health Insurance Plan ("Plan") is administered by the Minister of Health and Long-Term Care in accordance with the CHA.

Under the HIA, "insured persons" may, without charge, avail themselves of "insured services". Distinctions are drawn between "in-patients" and "out-patients". The regulations to the HIA define these terms as follows:

> "in-patient" means a person admitted to and assigned a bed in a hospital in-patient area;
> . . .
> "out-patient" means a person who receives out-patient services and is not admitted to an in-patient area.[14]

In-Patient Coverage

In the case of a hospital in-patient, the range of insured services is set out in the regulations to the HIA:

> 7. Subject to section 10, the in-patient services to which an insured person is entitled without charge are all of the following services:
> . . .
> 4. *Drugs, biological and related preparations that are prescribed by an attending physician, oral and maxillofacial surgeon or midwife in accordance with accepted practice and administered in a hospital*, but not including any proprietary medicine as defined from time to time by the regulations made under the Food and Drugs Act (Canada).[15] (emphasis added)

The general rule is that while drugs are provided to hospital in-patients, they are not covered once the individual is discharged from hospital, or obtains services at first instance as an out-patient. The eligibility of an insured person to receive insured services in a hospital is also subject to certain criteria. These include having been admitted as an in-patient on the order of a

[13] Section 1.1 of O.Reg. 552 to the HIA, amended to O.Reg. 345/01, defines "resident" to include individuals who are ordinarily resident in Ontario with Canadian citizenship or landed immigrant status; and others. In 1994, the definition of "resident" was amended, resulting in approximately 60,000 individuals being excluded from OHIP coverage. A Charter challenge was brought by a group that was adversely affected by the regulatory change, but it was ultimately unsuccessful: see *Clarken v. Ontario (Health Insurance Plan)* (1998), 52 C.R.R. (2d) 74 (Ont. Div. Ct.); see also, *Irshad (Litigation Guardian of) v. Ontario (Minister of Health)* [2001] O.J. No. 648 (Ont. C.A.) In both of those cases, the court acknowledged the fiscal pressures faced by governments of the day, and upheld their right to amend the definition of "resident".

[14] O.Reg. 552, s. 1(1).

[15] O.Reg. 552, s. 7; *Food and Drugs Act,* R.S.C. 1985, c. F-27, as amended.

physician; and being referred to the hospital as an out-patient by a physician for particular service, an osteopath or chiropractor for X-rays, or an oral and maxillofacial surgeon, for enumerated laboratory, radiological or diagnostic procedures.[16]

Out-patient coverage

> 8(1) The out-patient services to which an insured person is entitled without charge are all of the following services:
> . . .
>
> 5. The hospital component of all other out-patient services, including the use of an operating room and anesthetic facilities, surgical supplies, necessary nursing service, meals required during a treatment program *and the supplying of drugs, biologicals and related preparations that are prescribed in accordance with accepted practice by a physician on the medical staff, a midwife on the midwifery staff or an oral and maxillofacial surgeon on the dental staff of a hospital and that are administered in the hospital,* but not including,
>
> i the provision of any proprietary medicine as defined from time to time by the regulations made under the *Food and Drugs Act* (Canada),
> *ii the provisions of medications for the patient to take home,*
> iii the diagnostic services performed to satisfy the requirements of third parties such as employers and insurance companies, and
> iv *visits solely for the administration of drugs, vaccines, sera or biological products*.[17] (emphasis added)

Exceptions to the rule against medication coverage for out-patients

1. Subsection 8(2) provides that despite the exclusion of coverage for medications set out in para. (ii) above, in specific circumstances, an out-patient will be entitled without charge to specific medications for use in the home. At present, 12 medications or categories of medications (e.g., where the drug is not specifically named, but is deemed " . . . a medication for the treatment of . . .") are set out by way of a chart. An example of a condition for insured service would be that the medication must be available in a hospital in Ontario, and/or be prescribed by a physician on the medical staff of a hospital graded as a particular Group (e.g., S, T) under the PHA.

2. Subsection 8(3) of the regulation creates a second exception to the exclusion of coverage to insured persons for hospital visits to administer drugs, vaccines, sera or biological products, as set out in para. (iv) above. An out-patient visit for which an insured person is

[16] O.Reg. 552, as amended, s. 11(1).
[17] O.Reg. 552, s. 8(1), as amended.

> entitled without charge includes a visit that is solely for the administration of one of the 12 medications or categories of medications discussed above, provided that specific criteria are met (e.g., the medication is prescribed by a physician, etc.).

Special Drugs Program

Where the exceptions listed above are met, the Ontario Ministry of Health and Long-Term Care (MOHLTC) will pay the cost of medications to out-patients, through its Special Drugs Program (SDP), a division of its Drug Programs Branch. The SDP covers the full cost of select out-patient drugs used in the treatment of specific conditions, and under specific circumstances.

The SDP covers:

- many drugs for the treatment of cystic fibrosis and thalassaemia;
- AZT, ddI, ddC and pentamadine for people who are HIV positive;
- Erythropoietin (EPO) for people with end stage renal disease;
- Cyclosporine for people who have had a solid organ or bone marrow transplant;
- human growth hormone for children with growth failure;
- Clozapine for treatment of schizophrenia;
- Alglucerase for people with Gaucher's Disease.[18]

An insured person is entitled to services without charge as both an in- or out-patient in any hospital listed in Schedule 2 to the regulation; and in a hospital graded under the PHA as a Group A, B, C, E , F, G, J or R hospital.[19]

Finally, section 28 of the HIA states:

> Any amounts payable to or on behalf of an insured person under the Plan in respect of insured services provided by or in a hospital or health facility may be paid in the form of the payment by the Province of all or any part of the annual expenditures of such hospital or health facility, where such payment by the Province is authorized under any Act.

The PHA provides the authority contemplated in section 28.

3. Public Hospitals Act[20]

The Minister of Health and Long-Term Care is granted an important discretion in subsection 5(1) of the PHA:

[18] On-line at: http://www.gov.on.ca:80/MOH/english/pub/drugs/specdrug.html (accessed November 17, 2001).
[19] O.Reg. 552, s. 9(1), as amended.
[20] R.S.O. 1990, c. P.40 [hereinafter "PHA"].

> The Minister may pay any grant, make any loan and provide any financial assistance to a hospital if the Minister considers it in the public interest to do so.

Hospitals are classified under the PHA, and are graded accordingly.

4. Drugs Covered Through Cancer Care Ontario

The New Drug Funding Program was established in 1995. The goal of the program is to provide equal access to new effective agents for eligible patients throughout the province. As a result, access to expensive drugs is not limited by place of residence or a health care facility's drug budget and new treatments are introduced in a standard manner on a provincial basis.

A Policy Advisory Committee recommends to Cancer Care Ontario (CCO) the drugs and the eligibility criteria for funding, after reviewing Evidence-based Guidelines that are developed by eleven multi-disciplinary provincial disease site groups that are part of the CCO Program in Evidence-based Care.

CCO is responsible for managing the budget on behalf of the Ministry of Health and Long-Term Care and reimbursing cancer centres and hospitals for the drug costs of those patients that meet the eligibility criteria. During 2000/2001 a budget of 37.5 million funded 14 drugs for 24 indications.[21]

Analysis

1. Drug Coverage – A Costly Gap Identified

It should be noted that while Canada's publicly funded health care system is often deemed to be comprehensive, there are many instances in which individuals, or their private insurers, must pay for particular health services, including long-term care and most prescription drugs. The burden on public hospitals to pay for drug therapies out of their global budgets takes on added significance in the face of a dramatic increase in spending on drugs. In its landmark 15-year review of national drug expenditures, the Canadian Institute for Health Information (CIHI) stated:

> In summary, drug expenditures account for an increasing share of total health expenditures. Given that the drug index(es) have remained relatively stable since the early 1990s, it appears that increased utilization and the entry of new drugs are the main factors behind the increase in drug expenditures.[22]

---

[21] Information taken directly from CCO's website: http://www.cancercare.on.ca/treatment/newdrugs.html, (accessed November 17, 2001).

[22] *Drug Expenditures in Canada 1985-2000* (Ottawa: Canadian Institute for Health Information, 2001) Executive Summary at *iii*.

For the year 1998, the CIHI study found that the cost of drugs dispensed in hospitals reached $1 billion.[23]

Public hospitals in Ontario have collectively expressed their concerns about the impact of having to pay for drug therapies through their global budgets. In its recent submission to the Commission on the Future of Health Care in Canada,[24] the Toronto-based University Health Network (UHN) pointed to the impossible situation faced by teaching hospitals in relation to non-insured services:

> There is pressure to keep patients in hospital after their acute phase because health insurance often does not cover services outside the hospital (e.g., drugs, home nursing care, rehabilitation, homemaking services).[25]

The UHN submission further notes that teaching hospitals ". . . are significantly affected by the high costs of new drugs given their highly specialized programs." [26] On the topic of its legal duty to provide medically necessary services that are insured for in-patients, the UHN stated:

> The *Canada Health Act* covers all "medically necessary" hospital and physician services. Many elements of the health care system (e.g., drugs, long term care) are not covered under this act, which results in hospitals being pressured to provide services to patients who might otherwise be treated outside the system.[27]

The UHN also brought to the attention of the Romanow Commission that at the time of making its submission in September, 2001, it had not yet received final notice from the Ontario Ministry of Health and Long-Term Care "regarding funding levels for fiscal 2002."[28]

In the opinion of one legal scholar, the emphasis of the *Canada Health Act* on hospital and physician-based services is contrary to the recent move to a continuum of care, as evidenced through the provision of integrated and comprehensive health services:

> Advances in technology have revealed the system's inflexibility. There is now less need for health care services to be delivered in hospitals and institutions and there is an increased need for drugs prescribed for use outside the hospital and home care services, neither of which is consistently publicly-funded. Inconsistent funding thus makes it difficult to have an integrated and comprehensive system that allows substitution between different types of health services and goods.[29]

Governments continue to "delist" formerly insured services, and in some cases, add new services as government policy dictates. Conversely, some publicly funded services, while not mandated

[23] *Ibid,* Figure 4, p. 14.
[24] *Sub. nom,* "Romanow Commission".
[25] *Supra,* note 1 at 6.
[26] *Supra*, note 1 at 14.
[27] *Supra*, note 1 at 14.
[28] *Supra*, note 1 at 14, "The View From the Front Lines".
[29] C. Flood, *supra*, note 8 at 9.

under the *Canada Health Act,* are nonetheless provided by provincial governments. Examples in Ontario are the Drug Benefits Program and Trillium Drug Program, which provide almost fully subsidized prescription medication to specific groups, e.g., individuals receiving social assistance, seniors, recipients of homecare services, and residents of nursing homes, homes for the aged and homes for special care.[30]

2. Responses by Legislatures

Under the HIA, the Lieutenant Governor in Council is granted extensive regulation-making authority to administer the Act. It is clear that the HIA provides sufficient authority for the provincial government to govern "insured services, including specifying those services that are not insured services", as well as governing both the fees payable and the payments to be made for the insured services.[31] Discretion also exists under the PHA for the Minister of Health and Long-Term Care to pay grants or financial assistance to public hospitals where it is in the public interest to do so. Because this is a permissive and not a mandatory provision, an argument that the Minister must take on the costs of out-patient drug coverage would likely be unsuccessful, unless the Minister's discretion could be proven to have been improperly exercised.

At present, on the authority of s. 5 of Regulation 552 to the HIA, hospitals must provide drug coverage to out-patients, including the prescribed supply of "drugs, biologicals and related preparations" unless the out-patient visit is solely "for the administration of drugs, vaccines, sera or biological products." There are exceptions to this rule (e.g., the twelve medications or categories of medications named under s. 8(1) of the Regulation, and any drugs included in the "solely for administration" category of out-patients, if those drugs are covered through s. 8(2) of the Regulation. Under those conditions, the Ministry of Health and Long-Term Care will pay for the drugs through its Special Drugs Program.

The issues that teaching hospitals must delineate are:

1. Which out-patient visits are solely for the administration of a drug.
2. If the visit is not solely for the administration of a drug, but drugs are provided in hospital (e.g., ancillary to a surgical procedure in an out-patient clinic), the hospital must bear the cost of the drug.
3. If the visit is solely for the administration of a drug, whether the drug falls under the exceptions set out in s. 8(1) or 8(2) of Regulation 552 to the HIA (in which case, it will be covered through the Special Drugs Program).
4. If the visit is solely for the administration of a drug that does not fall under the exceptions, it is not an insured service to which the individual is entitled HIA, and the individual or their insurer must pay for the drug.

[30] These prescription medications must be listed in Ontario's *Drug Benefit Formulary*; failing that, an expert committee will assess whether the MOHLTC should pay for a particular medication. See generally, http://www.gov.on.ca/health/english/program/drugs/drugsfaq_dt.html.
[31] HIA, s. 45(1)(e)-(g) inclusive.

3. Responses by Courts

a) Tort Law

There is well-established caselaw before the Supreme Court of Canada that decisions taken by public authorities will not be subject to review by the courts where they were made for policy reasons. In *Brown v. British Columbia* and *Just v. British Columbia,*[32] panels of the Supreme Court found that policy decisions of government are to be afforded a degree of deference by the courts. Both cases unfolded well outside the realm of health services, in that each dealt with the issue of the public authority's duty to maintain safe highways.

Speaking for the majority in *Just*, Cory J. considered the approach that should be taken by courts when considering the liability of government agencies in tort actions. Even if it were possible to establish that a duty of care exists, the claim will not necessarily be successful:

First, the applicable legislation must be reviewed to see if it imposes any obligation upon the respondent to maintain its highways or, alternatively, if it provides an exemption from liability for failure to so maintain them. Secondly, it must be determined whether the province is exempted from liability on the grounds that the system of inspections, including their quantity and quality, constituted a "policy" decision of a government agency and was thus exempt from liability.[33]

A policy decision of government will shield it from liability, whereas an institutional decision will not:

The distinction between policy and operational factors is not easy to formulate, but the dividing line between them will be observed if we recognize that a public authority is under no duty of care in relation to decisions which involve or are dictated by financial, economic, social or political factors or constraints. Thus budgetary allocations and the constraints which they entail in terms of allocation of resources cannot be made the subject of a duty of care.[34]

Finally, the court stated:

> The characterization of such a [policy] decision rests on the nature of the decision and not on the identity of the actors. As a general rule, decisions concerning budgetary allotments for departments or government agencies will be classified as policy decisions.

Further, it must be recalled that a policy decision is open to challenge on the basis that it is not made in the bona fide exercise of discretion. [35]

---

[32] *Supra*, note 4.
[33] *Just, supra,* note 4 at para. 13 (Q.L.).
[34] *Ibid.,* at para. 19 (Q.L.).
[35] *Ibid.,* at para. 29 (Q.L.).

Based on the caselaw related to government liability and ministerial discretion, it is my view that In order for a claim in tort law to be successful against the government for the failure to provide coverage for specific drug therapies, a party would have to show:

- that even if there was proper statutory authority to allow such a decision to be made, the decision was an operational decision and not a policy decision, and a duty of care was therefore established; or
- if it was a policy decision, the decision was made either in bad faith or there was an improper exercise of discretion.

In my view, on the facts provided, it is unlikely that such a suit would be successful.

b) Charter challenges

In a 1997 decision of the Supreme Court, the application of the Charter was determined to extend to hospitals. While public hospitals are not part of government and therefore not automatically subject to the Charter, *Eldridge v. British Columbia*[36] has changed the way hospital actions are scrutinized in relation to the delivery of health services:

Hospitals implement a specific government policy and objective, namely that residents will be guaranteed access to a range of medically necessary services. In discharging that responsibility, hospitals are subject to the Charter; government cannot evade its responsibility to ensure Charter compliance by the expedient of delegating the power to carry out its objectives.[37]

Eldridge was a case on appeal from the British Columbia Court of Appeal involving two deaf patients and their request for funded interpreter services. The named appellant, Robin Eldridge, was not provided with a government-funded interpreter through the course of a number of medical procedures in hospital. The second appellant, Linda Warren, delivered twins prematurely without the benefit of an interpreter. Each claimed that these omissions infringed the equality rights protected under s. 15(1) of the Charter. While the B.C. legislation is slightly different than Ontario's, parallels may be drawn:

> Consequently, the fact that the *Hospital Insurance Act* does not expressly mandate the provision of sign language interpretation does not render it constitutionally vulnerable. The Act does not, either expressly or by necessary implication, forbid hospitals from exercising their discretion in favour of providing sign language interpreters. Assuming the correctness of the appellants' s. 15(1) theory, the *Hospital Insurance Act* must thus be read so as to require that sign language interpretation be provided as part of the services offered by hospitals *whenever necessary for effective communication.* As in the case of the *Medical and Health Care Services Act*, the potential violation

[36] *Supra,* note 6.
[37] J. Gilmour, "Death & Dying" in *Canadian Health Law Practice Manual*, M.J. Dykeman, ed. (Toronto: Butterworths, 1999) at §8.122.

> of s. 15(1) inheres in the discretion wielded by a subordinate authority, not the legislation itself. (emphasis added).[38]

On that basis, the teaching hospitals could consider taking the position that the failure to fund certain out-patient drug therapies constitutes an infringement of the individual's s. 15(1) right to equality, to which they do not want to be a party. However, such a challenge is typically brought by the individual who is alleging that they have been adversely affected by a law or government action.

The most obvious target for such a Charter challenge could be the government decision to fund certain out-patient drug therapies, and not others, through the Special Drugs Program (SDP). However, from a strategic perspective, a teaching hospital would have to consider very carefully how prudent it would be to force expanded drug coverage on the basis of *Eldridge.* The concern is that such a challenge could create a 'floodgates' effect'; there is at least a risk that this could result in hospitals having to pay for more services out of their global budgets.

.

[38] *Supra*, note 6 at para. 34 (Q.L.)

Figure 4. Example CCO Eligibility Form

ELIGIBILITY FORM FOR THE ADJUVANT TREATMENT OF BREAST CANCER

Paclitaxel administered as part of the AC-Taxol regimen O
OR
Epirubicin administered as part of the CEF regimen O

1. **PATIENT SURNAME** _____ 2. **GIVEN NAME** _____

3. **DATE OF BIRTH** __ __ (Day) • __ __ (Month) • __ __ (Year) 4. **HEALTH INSURANCE NUMBER** _____

5. **CENTRE** (Circle correct response)
1 Hamilton 2 Kingston 3 London 4 Ottawa Civic
5 Ottawa General 6 Sudbury 7 Thunder Bay 8 Toronto-Sunnybrook
9 Windsor 10 PMH 11 Other (specify below)

Other : _____

6. **ATTENDING PHYSICIAN** _____

If not a Cancer Centre physician, please indicate your phone number _____

7. **ELIGIBILITY** (Patient must meet criteria a or b)

a. Patient has node positive breast cancer O Yes

b. Patient has high risk node negative breast cancer O Yes
High risk features include:

Large tumour size	Specify _____	O Yes
High tumour grade	Specify _____	O Yes
LVIN		O Yes
ER negative		O Yes
PgR negative		O Yes
Her-2 neu positive		O Yes
Age less than 40		O Yes
Other	Specify _____	O Yes

8. **OTHER INFORMATION**
Patient is: (i) pre-menopausal OYes
OR
(ii) post-menopausal O Yes

9. **PLANNED DATE OF FIRST DOSE** __ __ (Day) • __ __ (Month) • __ __ (Year)

Recommended doses: Paclitaxel: 175 mg/m^2 every 3 weeks x 4 cycles
Epirubicin: 60 mg/m^2 on day 1 and 8 of a 4-week cycle x 6 cycles

_____ __ __ (Day) • __ __ (Month) • __ __ (Year)
Signature of prescribing physician

This completed form should be sent to the pharmacy and be forwarded with the monthly invoice to:
Mrs. Marilyn Nefsky, Cancer Care Ontario, 620 University Avenue, Toronto, Ontario M5G 2L7
Revised January 18, 2001

Table 22. Drugs and Indications covered under the CCO's New Drugs Funding Program
(accessed September 2001 at: http://www.cancercare.on.ca/treatment/newdrugs.html)

Clodronate
IV Clodronate for Metastatic Breast Cancer

Docetaxel
Docetaxel for Metastatic Breast Cancer
Docetaxel for Non-small Cell Lung Cancer (2nd line)

Epirubicin
Epirubican for Adjuvant Treatment of Breast Cancer(CEF)

Gemcitabine
Gemcitabine for Carcinoma of Bladder or Urothelium
Gemcitabine for Non-Small Cell Lung Cancer
Gemcitabine for Pancreatic Cancer

Interferon
Interferon for Melanoma

Irinotecan
Irinotecan for Colorectal Cancer

Liposomal Anthracyclines
Liposomal Anthracyclines for HIV-positive Kaposi Sarcoma

Paclitaxel
Paclitaxel for Adjuvant Treatment of Breast Cancer (AC-Taxol)
Paclitaxel for Advanced Ovarian Carcinoma (1st line)
Paclitaxel for Advanced Ovarian Carcinoma (2nd or 3rd line)
Paclitaxel for Metastatic Breast Cancer

Pamidronate
Pamidronate for Metastatic Breast Cancer
Pamidronate for Plasma Cell Myeloma

Raltitrexed
Ralitrexed for Colorectal Cancer

Rituximab
Rituximab for Diffuse Large B Cell Lymphoma (DLBCL)
Rituximab for Lymphoma

Topotecan
Topotecan for Advanced Ovarian Carcinoma

Trastuzumab (Herceptin)
Trastuzumab for Metastatic Breast Cancer

Vinorelbine
Vinorelbine for Metastatic Breast Cancer
Vinorelbine for Non-Small Cell Lung Cancer

Table 23. PAC's Evaluation Matrix for New Drugs

Evaluation Criterion	Example 1: *Vinorelbine in Advanced Non–Small-Cell Lung Cancer*	Example 2: *Bisphosphonates in Breast Cancer*
*Highest level of benefit**	2	3
Magnitude of benefit	6-8 weeks	30-40% reduction in risk of hip fracture or need for radiotherapy
*Quality of evidence for benefit***	2	1
Alternatives	standard therapy and other new drugs	none
Cost per month	$700	$240
Avg. duration of treatment	2 months	12 months
No. of patients projected per year	900	400
Estimated annual system costs	$1,260, 000	$1,152,000

Adapted from: Pater J et al. J Clin Oncol 2001;19:3392-6.

*Hierarchy of benefits: 1) cure; 2) prolongation of survival; 3) relief/prevention of symptoms/complications of disease; 4) improved quality of life; 5) reduction in symptomatic toxicity compared with standard therapy; 6) prolongation of disease-free survival; 7) tumor shrinkage.

**Hierarchy of evidence: 1) multiple randomized trials or meta-analysis; 2) single randomized trials of reasonable size; 3) small randomized trial; 4) data from phase II trials.

APPENDIX V. QUEENSLAND HEALTH RESOURCES

Figure 5. Queensland Standard Drug Listing Example

PREPARATION	STANDARD PACK	RESTRICTIONS
Includes amendments current at 1/10/2001		
A		
ABACAVIR SULFATE:		
Tablet 300mg	60	For use in accord with Highly Specialised Drugs Program indications.
Oral Solution 20mg per mL, 240mL	1	
ABCIXIMAB:		
Injection 40mg in 20mL	1	Interventional Cardiologists for complex angioplasty.
ACAMPROSATE CALCIUM:		
Tablet 333mg	180	Drug and alcohol treatment physicians for use with a comprehensive treatment program for alcohol dependence with the goal of maintaining abstinence.
ACARBOSE:		
Tablet		Specialist Staff and Country Medical Superintendents for non-insulin dependent diabetics with inadequate control despite diet, exercise and maximal tolerated doses of other anti-diabetic agents.
50mg	90	
100mg	90	
ACEDAPSONE:		
Injection 150mg/mL, 4.5mL	1	Treatment of leprosy.
ACETAZOLAMIDE:		
Injection 500mg	1	
Tablet 250mg	100	
ACETIC ACID:		
Ear Drops 3% in Propylene Glycol, 15mL	1	
Solution 2%, 100mL	1	
Solution 3% (Green), 2L	1	
Solution 6%,		
200mL	1	
2L	1	
ACETYLCHOLINE – MANNITOL:		
Eye Drops 10mg - 50mg per mL, 2mL	1	
ACETYLCYSTEINE:		
Injection 2g in 10mL	10	For management of paracetamol overdose.
Solution 20%, 10mL	5	Specialist Staff and Country Medical Superintendents.

1

APPENDIX V. QUEENSLAND HEALTH RESOURCES

Figure 6. Queensland SDL Request Form

REQUEST FOR APPROVAL OF ADDITIONAL DRUGS FOR HOSPITAL USE AND POSSIBLE INCLUSION IN QUEENSLAND HOSPITALS STANDARD DRUG LIST

Addition of new drugs to the Standard Drug List has implications for patient care and hospital budgets. If inadequate financial provision is made, addition of new drugs can result in cut backs of funding for other services. Data on implication of change for pharmacy or other budget is important & may have relevance to restriction or speed of approval. To enable a balanced decision to be made, information on clinical benefits and cost implications is needed. If all data requested on this form is not supplied delays in consideration may result.

It is recommended that a request for addition to the Standard Drug List be submitted to the Queensland Hospitals Drug Advisory Committee through the local Medical Superintendent.

Completed Form Should Be Sent To: The Adviser in Pharmacy
Executive Secretary, QHDAC
Queensland Health
147-163 Charlotte Street,
BRISBANE QLD 4000

_____ ITEM NO.:

1.GENERIC OR APPROVED NAME:

2.PROPRIETARY NAME:

3.DOSAGE FORM OR FORMS REQUESTED:

4.MANUFACTURER:

5.SPECIFIC PHARMACOLOGICAL ACTIONS OR USES WHICH JUSTIFY THE NEED FOR THIS PREPARATION:

6.REASONS WHY THIS DRUG IS SUPERIOR TO OTHER AVAILABLE PREPARATIONS (IF APPLICABLE):

7.WILL THIS DRUG REPLACE FULLY OR PARTLY ANY DRUG PRESENTLY AVAILABLE ON THE STANDARD DRUG LIST **(If not, how were patients managed previously?)**:

8.SHOULD THE DRUG BE:
AVAILABLE FOR GENERAL USE
RESTRICTED TO SPECIALIST STAFF
RESTRICTED TO SPECIALIST STAFF & COUNTRY MEDICAL SUPERINTENDENTS
OR
HAVE MORE SPECIFIC RESTRICTIONS:

Please describe any identifiable subgroup of patients most likely to benefit from availability:

ANTICIPATED USAGE: PLEASE PROVIDE THE USAGE INFORMATION REQUESTED ON THE NEXT PAGE.

9.ANTICIPATED USAGE: (Indication of likely effect on own clinic and extrapolation to larger population would assist when item is considered) or (Estimate of likely usage in your hospital in the first year?)

Likely No of patients in Clinic: In State:

Usual Daily Dose:

Usual duration of therapy:

Approximate annual usage per patient:

Additional information:

10.MEDICAL SUPERINTENDENT COMMENTS:

11.CHIEF PHARMACIST COMMENTS:

12.PRICE (Include detail of pack size etc):

13.ADEC APPROVED INDICATIONS:

14.PBS STATUS:

15.POTENTIAL CONFLICT OF INTEREST STATEMENT

I certify that I am aware of no potential conflict of interest which may arise in respect of this application for inclusion of a drug on the Standard Drug List for Queensland Hospitals, **except as listed below**. (Please note that it is not assumed that any of the activities listed necessarily constitute a conflict of interest and disqualify the applicant from making submissions to QHDAC).

I may have a conflict of interest for the following reason/s:
[e.g. Receipt of research funds from a sponsoring company; Receipt of ex-gratia payments or consultancy fees from a sponsoring company; Overseas/interstate trips funded or subsidized by a sponsoring company; Personal or family shares in the company sponsoring the product/s (or competing product/s) for which application is made].

.....

.....

.....

REQUESTED BY:

POSITION:

HOSPITAL:

.....
(SIGNATURE) (DATE)

NB: APPLICANT PLEASE ATTACH RELEVANT DOCUMENTS EG: CLINICAL PAPERS, DRUG PROFILE

g:\pas\qhdac\sdlapptl.doc 7/97

Figure 7. Queensland HSD Request Form

REQUEST FOR HIGHLY SPECIALISED DRUG FORMS

To minimise unnecessary paper usage, it is proposed to send Highly Specialised Drug forms to hospitals only for those drugs they wish to claim for.

Please indicate forms required:-

- ☐ Abacavir
- ☐ Apomorphine
- ☐ Azithromycin
- ☐ Baclofen
- ☐ Cidofovir
- ☐ Clarithromycin
- ☐ Clozapine
- ☐ Cyclosporin Neoral
- ☐ Delavirdine
- ☐ Desferrioxamine
- ☐ Didanosine (DDI)
- ☐ Disodium Pamidronate
- ☐ Dornase Alfa
- ☐ Doxorubicin
- ☐ Efavirenz
- ☐ Epoetin Alfa (Erythropoietin)
- ☐ Filgrastim
- ☐ Foscarnet
- ☐ Ganciclovir
- ☐ Indinivar
- ☐ Interferon Alfa 2a
- ☐ Interferon Alfa 2b
- ☐ Interferon Gamma 1b
- ☐ Lamivudine
- ☐ Lamivudine & Zidovudine
- ☐ Lenograstim
- ☐ Mycophenolate
- ☐ Nelfinavir
- ☐ Nevirapine
- ☐ Octreotide
- ☐ Ribavirin & Interferon Alfa 2b
- ☐ Rifabutin
- ☐ Ritonavir
- ☐ Saquinavir
- ☐ Stavudine (d4T)
- ☐ Tacrolimus
- ☐ Valaciclovir
- ☐ Zalcitabine (DDC)
- ☐ Zidovudine (AZT)

Please print name and address clearly:

..... **(Authorised person's name)**

..... **(Position)**

..... **(Hospital)**

..... **(Address)**

.....

..... **(Contact phone No.)**

Return form to: Adviser in Pharmacy
Queensland Health
GPO Box 48
BRISBANE Q 4001

Phone: (07) 32341167
Fax: (07) 32340773

Alternatively these forms can be directly accessed (and printed) from Queensland Health Electronic Publishing Service at the Pharmaceutical Advisory Services Home page, http:// qhin.health.qld.gov.au/phs/pas

HSD Request Form –HSD/H95/HSD92000

Figure 8. Queensland HSD Supply Form (Sample)

Queensland Government
Queensland Health

PHARMACY REGISTER

DETAILS OF DOXORUBICIN (liposomal) SUPPLY

HOSPITAL ..... **MONTH** ..... **YEAR** .....

DATE	PATIENT/ PATIENT CODE	REGISTER NUMBER	HOSPITAL OF ORIGIN	THERAPEUTIC INDICATION	DATE THERAPY STARTED	QUANTITY DISPENSED Infusion 20mg/10ml			DRUG COST	PATIENT CO-PAYMENT

NOTE: Alternative forms or processes which provide the required data may be used.

RESTRICTION: Treatment of AIDS-related Kaposi's sarcoma in patients with CD4 cell counts of less than 200 per mm^3 and extensive mucocutaneous or visceral involvement - for eligible out-patients

Signature of Chief Pharmacist ..... Date. .....

FORM: Adox.1000

Figure 9. Queensland HSD Program Usage Report

Queensland Government
Queensland Health

HIGH COST/HIGHLY SPECIALIZED DRUG PROGRAM

USAGE REPORT

FOR PERIOD: / / TO / /

FOR DRUG: DOXORUBICIN (liposomal)

HOSPITAL: .....

DISTRICT: .....

SECTION 1.
OUTPATIENTS: ELIGIBLE FOR FUNDING (See Note 2)

NUMBER OF PATIENTS See Note 1.	DOSE FORM & STRENGTH	QUANTITY ISSUED	TOTAL COST OF DRUG SUPPLIED	PATIENT COPAYMENT $ GENERAL	CONCESS
	Susp for IV inf 20mg/10ml vial				
↑ Please indicate Number of Patients here					

NOTE 1: **The number of patients should be the total number of eligible out-patients using this drug for this period. It should not indicate number of dispensings, nor should patients on two strengths of the drug be counted twice.**

NOTE 2: **In Section 1 include only data on eligible out-patients covered by Commonwealth approved indications.**

APPROVED INDICATION:

☐ **Treatment of AIDS-related Kaposi's sarcoma in patients with CD4 cell counts of less than 200 per mm ^{3} and extensive mucocutaneous or visceral involvement.**

Form to be forwarded to Adviser in Pharmacy, Corporate Office, Queensland Health, GPO Box 48, BRISBANE, 4001 for three month periods to end of Sept, Dec, Mar, Jun (within 21 days).

Number of charts audited in this period.....

DATA COMPILED BY .....

DATA CERTIFIED CORRECT.....**(Authorised Officer) Date: / /**

FORM: Cdox.1000

Figure 10. Queensland HSD Program Eligibility Form

Queensland Government

HIGH COST/HIGHLY SPECIALIZED DRUG PROGRAM

ELIGIBILITY STATEMENT

HOSPITAL: .....

PATIENT'S NAME OR CODE: .....

MEDICAL RECORD NUMBER: .....

MEDICARE NUMBER: .....

DRUG: **DOXORUBICIN (liposomal)**

I confirm that the above patient

☐ **COMPLIES** ☐ **DOES NOT COMPLY**

with the following criteria for funding under Section 100 of the Pharmaceutical Benefits Scheme.

I agree to make the relevant records available for audit if required.

ELIGIBLE INDICATIONS FOR HCD PROGRAM
(Please tick appropriate box)

☐ Treatment of AIDS-related Kaposi's sarcoma in patients with CD4 cell counts of less than 200 per mm^3 and extensive mucocutaneous or visceral involvement.

NAME OF PRESCRIBER: ..... (please print)

SIGNATURE OF PRESCRIBER: ..... **DATE:** .....

[For office use]
CERTIFICATION OF AUDIT:
I certify that an audit of this patient's chart confirms compliance with approved HSD indications

Signed: ..... Date: .....

(This form should be completed by the prescriber and retained by the Pharmacy Department in order to attract funding under the HCD program. A photocopy of this form including pharmacy endorsement certifying chart compliance with approved indications should be made available to a patient returning to another hospital for supplies of drugs.)

FORM: E2dox.1000

Figure 11. Queensland HSD Program National Database Record (Example)

Queensland Government

HIGH COST/HIGHLY SPECIALIZED DRUG PROGRAM
ELIGIBILITY STATEMENT &
NATIONAL DATABASE RECORD

DRUG: DORNASE ALFA/PULMOZYME

Patient Name.....

Patient hospital identification number ..... Hospital .....

Date of Birth / / Sex ..... Medicare Number.....

Has patient agreed to participate in National Database ? Yes ☐ No ☐

Nebuliser (make/type) ..... Compressor pump .....

Number of days in hospital in past 6 months .....

Number of days unable to participate in usual daily activities in past 6 months .....

Exercise tolerance over past 6 months (please circle) Much worse / Worse / Unchanged / Better / Much Better

Date	
Weight	
Height	
FVC 1/sec	
FEV1 1/sec	
FEF25-75 1/sec	

Application is for (Please tick A, B or C if the relevant criteria are met)

☐ **(A) INITIAL 1 MONTH SUPPLY (TRIAL)**
Use by cystic fibrosis patients who satisfy all of the following criteria:
1. Patient has cystic fibrosis.
2. Patient is aged five years or over.
3. Patient shows evidence of chronic suppurative lung disease.
4. FVC ≥ 40% of predicted.
5. Patient's lung disease is currently stable.

☐ **(B) FIRST 6 MONTHS SUPPLY**
Criteria
1. Patient has shown an improvement in FEV1 ☐ 10% after first month of treatment.

$$\frac{\text{(FEV1 1/sec at 1 month - FEV1 1/sec at commencement) x 100\%}}{\text{FEV1 1/sec at commencement}} \quad \frac{\square - \square \times 100}{\square} = \square\%$$

☐ **(C) REPEAT 6 MONTH SUPPLY**

I confirm that the above patient complies with the criteria for funding under Section 100 of the Pharmaceutical Benefits Scheme and has agreed to the inclusion of their data in the National Database. I agree to make the relevant records available for audit if required.

Physician's name .....

Physician's signature..... Date.....

If not managed in cystic fibrosis unit: Unit consulted..... Specialist.....

This form should be completed by the prescriber and retained by the Pharmacy Department in order to attract funding under the HSD program. A photocopy of this form including pharmacy endorsement certifying chart compliance with approved indications should be made available to a patient returning to another hospital for supplies of drugs. If database participation is agreed, a further photocopy should be forwarded to:

NATIONAL CYSTIC FIBROSIS DATABASE, CENTRE FOR ADOLESCENT HEALTH,
2 GATEHOUSE STREET, PARKVILLE VIC 3052

FORM: E2dna1.1000

APPENDIX V. QUEENSLAND HEALTH RESOURCES

DORNASE ALFA PRESCRIBING CRITERIA AND FUNDING CONDITIONS

Prescribing criteria

Use by cystic fibrosis patients who satisfy all of the following criteria:

- are five years of age or older,
- have a FVC greater than 40% predicted for age, gender and height,
- have evidence of chronic suppurative lung disease (cough and sputum most days of the week, or greater than three respiratory tract infections of more than two weeks duration in any twelve months, or objective evidence of obstructive airways disease), and
- are participating in a four week trial as detailed below or have achieved a 10% or greater improvement in FEV1 (compared to baseline established prior to dornase alfa treatment) after a four week trial.

[It is highly desirable that all patients be included in the national cystic fibrosis patient database.]

Funding conditions

In order for patients to be eligible for participation in the HSD program, the following conditions must be met:

- Prior to dornase alfa therapy, a baseline measurement of FEV1 must be undertaken during a stable period of the disease. At or towards the end of the initial four weeks trial, patients must be reassessed and a further FEV1 measurement be undertaken (single test under conditions as above).
- Patients must be assessed at cystic fibrosis clinics/centres which are under the control of specialist respiratory physicians with experience and expertise in the management of cystic fibrosis and the prescribing or dornase alfa under the HSD program is limited to such physicians. If attendance at such units is not possible because of geographical isolation, management (including prescribing) may be by specialist physician or paediatrician in consultation with such a unit.
- The measurement of lung function is to be conducted by independent (other than the treating doctor) experienced technicians at established lung function testing laboratories, unless this is not possible because of geographical isolation.
- Patients who fail to meet a 10% or greater improvement in FEV1 after the four weeks treatment at the approved daily dose of 2.5mg daily, may have one further trial in the next twelve months but not before three months after the initial trial. [The provision for further testing in patients who fail the two trials in twelve months is to be reviewed at a later date.]
- Initial therapy is limited to 4 weeks' treatment with dornase alfa at a dose of 2.5mg.
- Following an initial six months' therapy, a global assessment is to be undertaken involving the patient, the patient's family (in the case of paediatric patients) and the treating physician(s) to establish that all agree that dornase alfa treatment is continuing to produce worthwhile benefits. [Dornase alfa therapy should cease if there is not general agreement of benefit as there is always the possibility of harm from unnecessary use.]
- Where there is documented evidence that a patient already receiving dornase alfa treatment would have met the criteria for subsidy (i.e. satisfied the criteria for the four week trial and achieved a 10% or greater improvement in FEV1) then the patient is eligible to continue treatment under the HSD program. Where such evidence is not available, patients will need to satisfy the initiation and continuation criteria as for new patients. [Four weeks is considered a suitable washout period.]
- Further reassessments are to be undertaken at six-monthly intervals.
- Other aspects of treatment, such as physiotherapy, are to be continued.
- In addition to the standard quarterly usage information, States and Territories will provide the following patient data:
  - Number of patients who commenced a 4 week trial within quarter
  - Number of patients who qualified for ongoing therapy within quarter
  - Number of patients receiving ongoing therapy at end of quarter

---

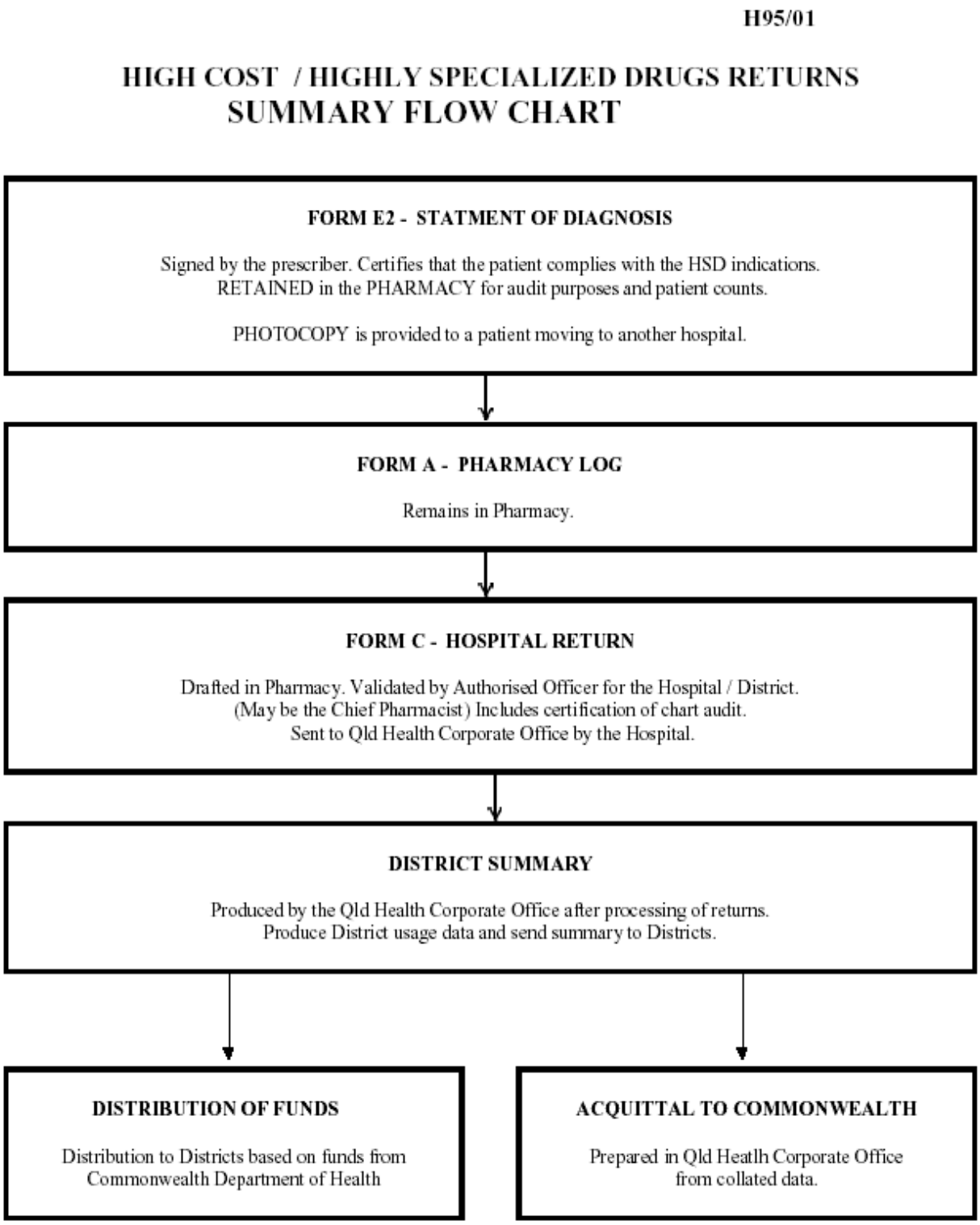
[For office use]

CERTIFICATION OF AUDIT:

I certify that a chart audit confirms compliance with approved HSD indications

Signed:..... Date: .....*FORM: E2dna2.900*

Figure 12. Queensland HSD Program Structure



APPENDIX VI. OCOTH Surveys

QUESTIONNAIRE I
(Self-administered)

Demographics

Hospital Name	
Contact Name	
Contact Phone	
Contact E-mail	

Are you a member of a buying group? Y / N

If yes, which ?

	Fiscal 1998	Fiscal 1999	Fiscal 2000
#Hospital Admissions			

Drug Expenditures

Overall	Total Hospital Budget	Rebates Received
Fiscal 1998		
Fiscal 1999		
Fiscal 2000		

Inpatient Drug Volumes and Expenditures

			Total Cost		
		Total Volume (units)	Hospital Budget	MOH Funding	Other
All Drugs	Fiscal 1998				
	Fiscal 1999				
	Fiscal 2000				
Antibiotics	Fiscal 1998				
	Fiscal 1999				
	Fiscal 2000				
Amiodarone	Fiscal 1998				
	Fiscal 1999				
	Fiscal 2000				
PPIs	Fiscal 1998				
	Fiscal 1999				
	Fiscal 2000				
H2RAs	Fiscal 1998				
	Fiscal 1999				
	Fiscal 2000				
LMWHs	Fiscal 1998				
	Fiscal 1999				
	Fiscal 2000				
Propofol	Fiscal 1998				
	Fiscal 1999				
	Fiscal 2000				

Atypical Antipsychotics	Fiscal 1998		
	Fiscal 1999		
	Fiscal 2000		
Epoietin	Fiscal 1998		
	Fiscal 1999		
	Fiscal 2000		
GP 2b/3a Inhibitors	Fiscal 1998		
	Fiscal 1999		
	Fiscal 2000		
Liposomal Amphotericin B	Fiscal 1998		
	Fiscal 1999		
	Fiscal 2000		

Others (please list) (specify costly agents)	Fiscal 1998		
	Fiscal 1999		
	Fiscal 2000		

Outpatient Drug Expenditures

			Total Cost			# Patients/
		Total Volume (units)	Hospital Budget	MOH Funding	Other	Admissions
All Drugs	Fiscal 1998					
	Fiscal 1999					
	Fiscal 2000					
biologic response modifying DMARD (e.g. infliximab)	Fiscal 1998					
	Fiscal 1999					
	Fiscal 2000					
Infliximab	Fiscal 1998					
	Fiscal 1999					
	Fiscal 2000					
Visudyne	Fiscal 1998					
	Fiscal 1999					
	Fiscal 2000					
Clodronate/ Pamidronate	Fiscal 1998					
	Fiscal 1999					
	Fiscal 2000					
Epoietin	Fiscal 1998					
	Fiscal 1999					

	Fiscal 2000		
Goserelin/ Leuprolide	Fiscal 1998		
	Fiscal 1999		
	Fiscal 2000		
Others (please list)	Fiscal 1998		
	Fiscal 1999		
	Fiscal 2000		

Section B: Drug Acquisition Costs (per Unit)

Omeprazole	10 mg	
	20 mg	
	40 mg	
Lansoprazole	15 mg	
	30 mg	
Pantoprazole	40 mg	
Ranitidine	75 mg	
	150 mg	
	300 mg	
	IV vial	
Enoxaparin	30 mg	
	60 mg	
	80 mg	
	100 mg	
Amiodarone	200 mg tablet	
	IV vial	
Propofol	10 mg/mL	
Liposomal Amphotericin B	50 mg vial	
Abciximab	2 mg/ml vial	
Tirofiban	12.5 mg powder	
	50 mcg/ml vial	

Section C: Are there any drugs for which you pay much LESS now than you did previously because they are now used less frequently? Please list.

Table 24. Survey 1 Results: Financial Indicators of Drug Utilization in OCOTH Hospitals.

Indicator	Sample Size	Mean (SD)	Median	Range
Hospital Expenditures (Year 2000)	8	$271 ($219) M	$212 M	($33 - $733 M)
Increase in Hospital Expenditures (1998-000)	8	25.9% (17.7%)	17.7%	(13.3-62.4%)
Hospital Admissions (Year 2000)	10	18,107 (9,719)	19,001	(1,973-39,226)
Increase in Hospital Admissions (1998-2000)	10	-1.7% (12.6%)	-3.6%	(-19.6%-25.0%)
Hospital Expenditure/Admission (Year 2000)	8	$14,570 ($5,536)	$13,626	($8,771-$23,953)
Increase in Hospital Expenditures/Admission (1998 2000), %	8	29.2% (18.6%)	24.0%	(13.7%-69.9%)
Total Drug Expenditures (Year 2000)	10	$10.5 ($9.0) M	$9.8 M	($1.3 - $33.4 M)
Increase in Total Drug Expenditures (1998-2000), %	9	19.5% (26.0%)	17.2%	(-13.7%-77.0%)
Total Drug Expenditures as a Proportion of Total Hospital Expenditures (Year 2000), %	8	4.1% (1.2%)	4.3%	(2.2%-5.0%)
Change in Total Drug Expenditures as a Proportion of Total Hospital Expenditures (1998-2000), %	7	-0.3% (1.06%)	-0.1%	(-1.4% - 1.4%)
Proportion of Total Drug Expenditures Accounted by External Funding (All years)	8	32.5% (18.3%)	38.0%	(4.5%-66.3%)
Increase in External Funding (1998-2000), %	8	45.9% (66.2%)	32.7%	(-36.5%-150%)
Net Drug Expenditures (Year 2000)	7	$6.2 ($5.0) M	$4.7 M	($2.7-$17.7 M)
Increase in Net Drug Expenditures (1998-2000), %	9	9.3% (13.6%)	8.0%	(-10.6%-29.1%)
Change in Net Drug Expenditures as a Proportion of Total Hospital Expenditures (1998-2000), %	7	-0.4% (0.48%)	-0.3%	(-1.1%-0.2%)

Net Drug Expenditures refers to those expenditures excluding external sources of funds such as rebates and MOH funding.

APPENDIX VI. OCOTH SURVEYS

QUESTIONNAIRE II
(Interviewer-administered)

SECTION 1: PTC Composition

SECTION 2: Scenario Questions

Your hospital's PTC is considering adding a high cost, high volume drug to its formulary that is expected to result in a high cost burden to the hospital (i.e. greater than 10% of the total hospital drug budget). Please address the following questions keeping in mind that you're now preparing for the PTC meeting.

1) How carefully do you feel this drug will be evaluated by your institution with respect to clinical and cost considerations? (1=not carefully at all, 10=extremely carefully)

2) How do you conduct the pharmacological and clinical evaluation of the drug? What is the formal process for evaluating the **quantity** and **quality** of evidence for use of the drug at your institution? Do you defer to subcommittees with special expertise in the clinical area in which the drug will be used?

Are you confident that the personnel reviewing the evidence have adequate training to critically search for and evaluate the available evidence and make clear recommendations? Please rate your level of confidence on a scale of 1 to 10. (1=not at all confident, 10=extremely confident)

3) Is there a formal process for evaluating the economic implications and cost-effectiveness of such a drug at your institution?

Are you confident that the personnel reviewing the cost-effectiveness aspects of the drug have adequate training to clearly understand economic evaluations? Please rate your level of confidence on a scale of 1 to 10. (1=not at all confident, 10=extremely confident)

You realize that one of the PTC members has presented materials on this drug on behalf of its manufacturer in the past several months.

4) How would your PTC deal with this situation?

5) Are there other conflict of interest situations that arise?
If yes, how are they usually handled?

Everyone agrees that the drug should be approved only for a specific indication. A prominent physician at your hospital argues for its use in several other indications. The evidence of efficacy at this time for these other indications is limited but does not suggest any advantage for this drug over existing alternatives.

6) How would your PTC handle this situation? What factors are considered?

The physician later presents several studies that suggest a favorable cost-effectiveness profile for use of the drug in the other suggested indications.

7) Assuming that the studies are convincing, how does the committee consider very expensive inpatient drugs that appear to be cost-effective (i.e. will subsequently save money in areas outside of the drug budget)?

The committee has decided to approve the use of this drug only for the original indication. However, the evidence for this drug is rapidly changing over time.

8) How do you develop drug use criteria defining appropriate use of the drug? Do economic considerations play a role in defining the drug's indications? How do you ensure that this drug will only be used for the approved indications at your hospital (e.g. Drug utilization evaluations) and how frequently are these exercises conducted? Do you have adequate resources to perform this function optimally?

9) Is there a process that outlines when a high cost burden drug would need to be reviewed for further indications or withdrawal as more evidence becomes available? Could you please describe this process?

Now assume that your hospital's PTC is considering adding a low cost, low volume drug to its formulary that is expected to result in a very low cost burden to the hospital (i.e. less than 1% of the total hospital drug budget). Please address the following questions.

10) Relatively speaking, how carefully do you feel this drug will be evaluated by your institution as compared to a high cost-burden drug with respect to clinical and cost considerations? (1=not carefully at all, 10=extremely carefully)

11) Would this drug be treated very differently relative to a high cost burden drug in its evaluation? If so, how?

Section 3: General Questions

1) What are the processes through which a drug and its indications are approved onto the formulary?

2) How does your PTC integrate its approvals and the resultant impact into a budget setting process (i.e. Are drug approvals made without any limitations on the drugs utilization?)? For example, some hospitals will not supply a drug if its utilization exceeds a predetermined amount.

3) How does the hospital currently acquire its inpatient drugs (e.g. Buying groups). To your knowledge, is there variability in the acquisition cost of particular drugs across hospitals?

4) What are the hospital's current funding sources for drugs (e.g. Global budget, cco, special drugs program [sdp], patient/out-of-pocket, private insurers) in the inpatient and outpatient settings?

APPENDIX VI. OCOTH SURVEYS

Inpatient:

Outpatient:

Are there any internal funding sources that offset the cost of some drugs?

5) Are there scenarios where cost or lack of budget or lack of patient's ability to pay is leading to a drug not being provided to a patient?

6) What are the types of cost-management strategies currently being undertaken to contain drug costs (e.g. Prior authorization requirements, dosing protocols, mandated intravenous to oral switch strategies)? Are they thought to be successful? Are there any other cost-containment strategies that are felt to be effective but are not being utilized due to limited resources?

7) How does your PTC balance the many different disorders for which drug therapies are available (i.e. Do drugs for certain disorders receive differential consideration?)

8) Does your PTC conduct a 'horizon scan' regularly for upcoming new drugs in preparation for future PTC meetings?

If so, how and how often?

What drugs are currently on your horizon?

9) As it pertains to drug utilization and expenditures, can you think of any features that clearly distinguish your hospital from others (e.g. Management strategies, differential costs)?

10) Are you willing to consider a central PTC that would represent all of the OCOTH hospitals in making formulary decisions for particular drug therapies that require specialized consideration? If so, how would you envision this committee functioning?

Note: Specify the types of decisions you feel a central PTC should undertake (e.g. All drugs vs. Particular drugs). Also note what the structure and function of such a committee would be.

11) Is your hospital so unique that it would require special considerations that would not be applicable to other hospitals when evaluating the effectiveness and cost-effectiveness of a drug therapy? If so, please explain.

Table 25. Survey 2 Results: Perceived care taken in evaluating high vs. low cost-burden drugs

<table>
<tr><td rowspan="4">QUESTION</td><td colspan="4">DISTRIBUTION OF RATINGS</td></tr>
<tr><td colspan="2">HI COST-BURDEN DRUG (>10% OF HOSPITAL DRUG BUDGET)</td><td colspan="2">LOW COST-BURDEN DRUG (<1% OF HOSPITAL DRUG BUDGET)</td></tr>
<tr><td colspan="2">HOW <u>CAREFULLY</u> DO YOU FEEL THIS DRUG WILL BE EVALUATED BY YOUR INSTITUTION WITH RESPECT TO CLINICAL AND COST CONSIDERATIONS?

WHERE...
1 = NOT CAREFULLY AT ALL,
10 = EXTREMELY CAREFULLY</td><td colspan="2">10.0: 7
9.5: 2
9.0: 5
8.0: 1
5.5: 1</td><td colspan="2">10.0: 4
9.5: 1
9.0: 1
8.0: 1
7.0: 1
6.5: 1
6.0: 2
5.0: 1
4.0: 1
2.5: 1
2.0: 2</td></tr>
<tr><td colspan="4">SUBSAMPLE (N = 8)</td></tr>
<tr><td><u>CLINICAL</u>

10.0: 4
9.5: 1
9.0: 3</td><td><u>COST</u>

10.0: 3
8.0: 3
7.0: 1
5.5: 1</td><td><u>CLINICAL</u>

10.0: 4
9.5: 1
9.0: 1
7.5: 1
6.5: 1</td><td><u>COST</u>

10: 2
8: 2
5: 2
3.5: 1</td></tr>
<tr><td>REVIEW/APPROVAL PROCESS FOR LOW VS. HIGH COST-BURDEN DRUGS</td><td colspan="4">• LOW COST-BURDEN "FAST-TRACKED"/"RUBBER-STAMPED"/SUBJECTED TO LESS FORMAL COST EVALUATION/LESS COMMITTEE DISCUSSION: 7
• EVALUATION OF THE LOW COST-BURDEN THE SAME, BUT POST-APPROVAL MONITORING LESS RIGOROUS: 1
• IF ANNUAL PROJECTION < $25 K, PTC ECONOMICS SUBCOMMITTEE NOT INVOLVED: 1
• IF ANNUAL PROJECTION < $5/25/50 K, PROGRAM DIRECTOR/SENIOR ADMINISTRATIVE APPROVAL NOT REQUIRED: 3</td></tr>
</table>

*WHEN RESPONDENTS GAVE A RANGE OF VALUES, THE MID-POINT OF THE RANGE WAS USED.

Table 26. Survey 2 Results: Perceived confidence in skills of personnel who evaluate new drugs

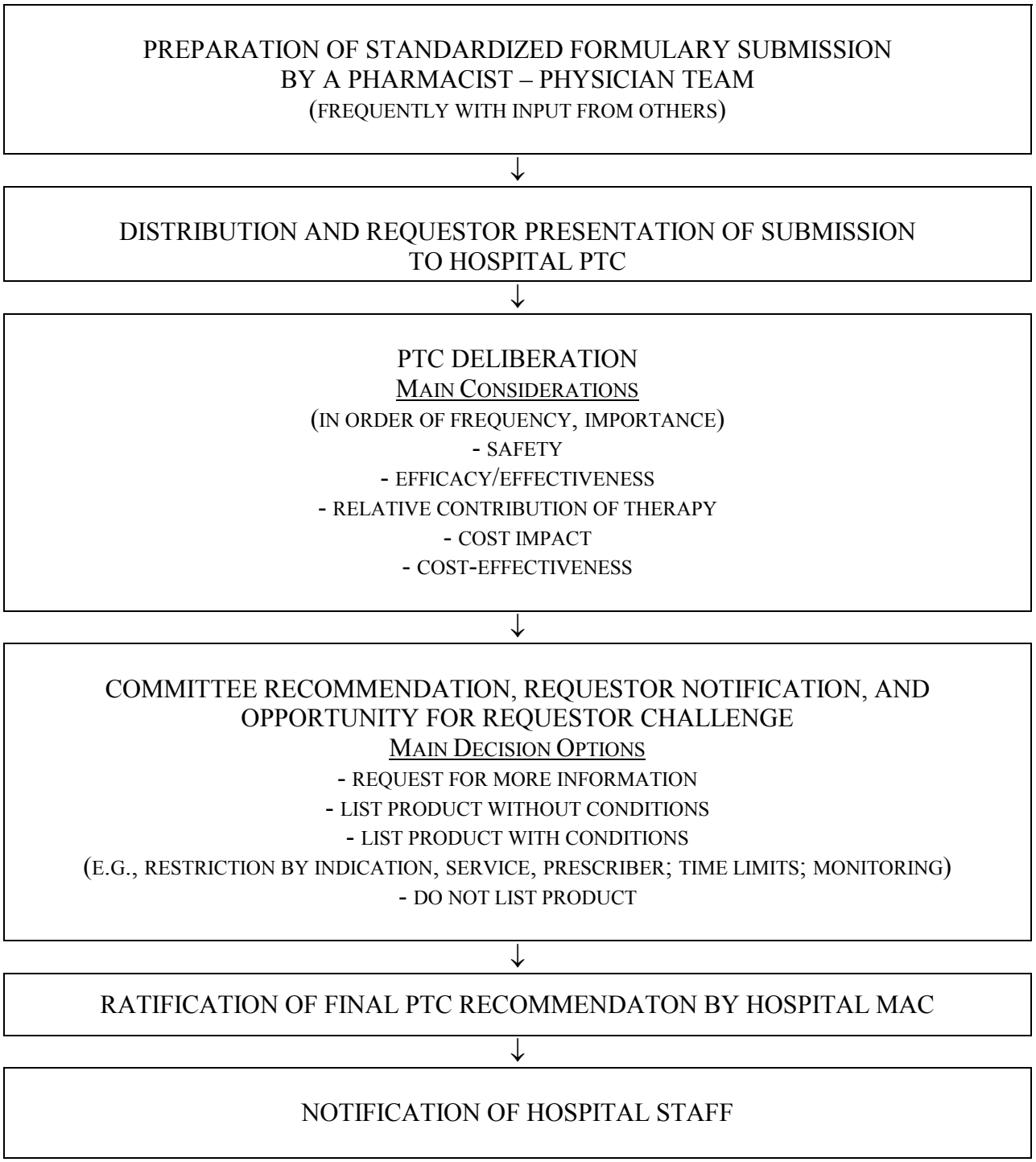
SKILL	DISTRIBUTION OF CONFIDENCE RATINGS *(WHERE 1 = NOT AT ALL CONFIDENT, 10 = EXTREMELY CONFIDENT)**
SEARCH FOR AND CRITICALLY APPRAISE AVAILABLE EVIDENCE AND MAKE CLEAR RECOMMENDATIONS	10.0: 6 9.5: 1 8.0: 5 7.0: 3 6.5: 1
REVIEW AND UNDERSTAND ECONOMIC EVALUATIONS	10.0: 3 9.5: 1 8.0: 2 7.0: 4 6.5: 1 6.0: 2 5.0: 1 4.5: 1 2: 1

* WHEN RESPONDENTS GAVE A RANGE OF VALUES, THE MID-POINT OF THE RANGE WAS USED.

Table 27. Survey 2 Results: Reported strategies for monitoring utilization, containing costs

STRATEGY	FREQUENCY *N (%)*
DOSING PROTOCOLS/GUIDELINES	9 (56.3)
PHARMACIST IN DISPENSARY REVIEWING ORDERS	7 (43.8)
MANDATED IV TO PO PROTOCOLS	6 (37.5)
AUTO-SUBSTITUTION	6 (37.5)
RESTRICTIONS BY INDICATION OR SERVICE	6 (37.5)
PHARMACIST CONSULTATION ON UNIT/WARD	5 (31.3)
AUTO-STOPS	4 (25.0)
PRE-PRINTED ORDER FORMS	4 (25.0)
OTHERS: PRE-AUTHORIZATION (E.G., FOR REMICADE); AUDIT AND FEEDBACK; LONGER-USE IV LINES; PAEDIATRIC ALIQUOTS; DRUG PREPARATION ONLY WHEN REQUIRED	1 EACH (6.3%)

Figure 13. Survey 2 Results: Common procedures for reviewing drugs for addition to Ontario Teaching Hospital formularies



APPENDIX VII. EVIDENCE FOR STRATEGIES TO IMPROVE PRESCRIBING PRACTICE IN THE HOSPITAL SETTING

Strategies designed to affect prescribing practice typically fall into one of three main categories: administrative; educational; or financial. Administrative interventions, such as highly managed formularies and prescribing restrictions, influence drug selection and utilization by creating barriers to undesired practices or reducing barriers to desired ones at a system level. Educational strategies include a broad range of interventions that are typically classified as being either active or passive. Examples of passive interventions include the distribution of printed educational materials, such as clinical practice guidelines, and didactic presentations. Systematic reviews of passive educational interventions have shown these to be largely ineffective.[96] However, when coupled with other, more active interventions, well developed clinical practice guidelines can provide a solid foundation for changing physician behaviour and improving patient outcomes. Among the more successful active co-interventions are face-to-face educational outreach or "academic detailing" visits[97]; audit and feedback interventions[98]; and computerized decision support.[99] Financial strategies, such as pharmacy risk contracts and bonus programs, provide financial incentives for particular prescribing decisions. Below we provide a sample of evidence supporting some of the more promising educational interventions.

1. Computerized Physician Order Entry and Decision Support

David Bates and colleagues at Brigham and Women's Hospital in Boston are world leaders in the study of computerized physician order entry (POE). Generally, their POE systems provide physicians with a menu of medications available on the formulary with default doses and a range of potential doses for each medication. Prescribers are required to enter the dosage, route, and frequency for each order. This ensures that orders are legible and provides opportunities to: display relevant lab results; provide reminders about possible concurrent medications or laboratory orders; and flag potential drug-allergy, drug-drug, and drug-laboratory interactions. In Bates' studies, POE reduced the number of medication errors with potential for harm by more than one-half.[100]

Like POE, computerized decision support (CDS) is software designed to aid in clinical decision making in which individual patients are matched to a computerized knowledge base for the purpose of generating patient-specific recommendations for consideration by the clinician. Where it differs from POE, however, is in its breadth of application. Readily available CDS now provides advice for a host of clinical functions, including drug dosing, diagnosis, and preventive care. In a recent review of CDS, effects on physician performance were assessed in 65 controlled trials, 43 (66%) of which found benefits. These included 9 of 15 studies of drug dosing systems, 1 of 5 studies of diagnostic aids, 14 of 19 studies of preventive care systems, and 19 of 26 evaluating CDS for other aspects of medical care.[99]

2. Pharmacist Order Review

While numerous studies have shown that retrospective review of medication orders prevents errors,[101], [102] relatively few, well-designed studies have assessed the impact of pharmacists' advice at the time of prescribing. In one such study, Leape et al. found that having a pharmacist

present on rounds as a full member of the patient care team in a medical ICU substantially reduced the rate of adverse drug events caused by prescribing errors.[103] Others also have shown that physician-pharmacist teamwork in ICUs,[104] on surgical units,[105], [106] and in hospital-based heart failure [107] and hypertension [108] clinics can have positive clinical and economic outcomes. Interestingly, Bond et al. [109] found that, after controlling for case mix in 934 US hospitals, hospital drug costs increased with increased staffing for pharmacy administrators, dispensing pharmacists, and pharmacy technicians, but decreased as a function of clinical pharmacy staff.

3. Audit and Feedback

Unlike traditional retrospective drug utilization reviews, which tend to focus on the prescribing patterns of a group or groups of prescribers, audit and feedback interventions typically consider the behaviour of individual prescribers. They also differ from computerized order entry or decision-support interventions in that, rather than give 'real-time' feedback regarding individual prescribing decisions, they provide a summary of prescribing behaviour over a specified time period, usually comparing the physician's practices or patient outcomes with those of peers or external standards and often providing specific recommendations for change. A recent review of comparative audit and feedback intervention studies drew five main conclusions:

- Audit and feedback interventions designed to affect specific prescribing behaviours need not necessarily be active or include supporting interventions to be effective.
- Targeted feedback interventions (i.e., those aimed at physicians with pre-specified prescribing problems) may be more likely to show positive outcomes than untargeted ones.
- Feedback programs sponsored by authoritative agencies, professional or regulatory bodies, or payers can be effective.
- Depending on the target behaviour, multiple reports on prescribing activity may not be needed to produce behaviour change.
- No studies could show whether the effects of feedback persist beyond 12 months.[110]

APPENDIX VIII. PHARMACOECONOMIC EVALUATIONS

Infliximab

While the introduction of infliximab, an anti-tumour necrosis factor monoclonal antibody, offers promise for the effective treatment of symptomatic perianal fistula associated with Crohn's disease (CD), the excessive cost of this treatment warrants careful use in order to maximize value in relation to other existing therapies. Although trial data suggest a 68% response rate and that benefits are realized within the first month after infusion (median time to response is 14 days), no long-term data currently exists on the rate of relapse after treatment with infliximab. The only published clinical trial in fistulizing patients lasted 18 weeks and reported that approximately 75% of patients lost their response within 4 months of initial treatment. On the outcomes side, the absolute difference in efficacy between infliximab and other available therapies such as 6-mercaptopurine (6MP) and metronidazole is difficult to assess given the lack of head-to-head clinical trials. Given this paucity of information, an explicit economic model estimating the relative clinical and economic effects may be more informative than implicit rationalizing.

A recently published USA-based cost-utility analysis[111] examined four treatment options for symptomatic perianal fistulae associated with CD, namely 1) combination 6MP/metronidazole, 2) 3 initial infusions of infliximab at weeks 0,2, and 6 with combination 6MP/metronidazole for treatment failures, 3) 3 initial infusions of infliximab at weeks 0,2, and 6 with episodic reinfusion for treatment failures, and 4) first line combination 6MP/metronidazole with treatment failures crossing over to 3 infliximab infusions with episodic reinfusion. The doses used in the evaluation were assumed to be for an average 70 kg person and were 5mg/kg of infliximab, 1000-1500 mg metronidazole every day, and 1.5 mg/kg every day. A Markov model with one-month cycle intervals was used to evaluate the costs and outcomes of care. This is perhaps the most appropriate model to evaluate such a problem. The analysis was not industry supported and was conducted from the perspective of the third party payer. The time horizon of the study was 1 year. Health states, upon consultation with gastroenterologists and colorectal surgeons, were defined to be initial fistula, persistent fistula (patients who do not improve in the 12-month period), improved fistula, abscess, and death. Pancreatitis and paresthesias were included as side effects of 6MP and metronidazole. The effectiveness parameter was 'fistula improvement' which was defined as either complete closure or symptomatic improvement (via an accepted rating scale or at least a 50% decrease in the number of draining fistula). Long-term data on the rate of relapse after treatment with infliximab is scarce. The probability of improvement after episodic reinfusion with infliximab, although unknown, was assumed to be equivalent to the mean probability of improvement after initial therapy. Fistula recurrence was assumed to occur at approximately 18% per month following infusion with infliximab based on very limited trial data. Variations of this estimate were examined using sensitivity analysis. The effects of 6MP and metronidazole were not assumed to be additive or synergistic but rather complimentary since patient usually do not respond to 6MP until 3 months following initiation and the effects of metronidazole are more immediate. Therefore, the monthly probability of fistula improvement was based on data from metronidazole studies whereas the monthly probability of fistula recurrence was based on data from studies of 6MP and metronidazole. Although probably unnecessary given the short time horizon of this evaluation, both costs and benefits were discounted at 3% per annum. Preference weights were directly elicited from 32 CD patients (17 fistulizing and 15 nonfistulizing) and 20 healthy subjects using the standard gamble technique.

Costs were derived from a single academic centre, namely the University of Virginia Clinical Data Repository and were based on hospital cost- Charge ratios. While this method of costing provides only estimates rather than actual costs, it was used consistently for each comparator and sensitivity analyses were conducted on all variables using tornado diagrams. The primary type of sensitivity analysis used was one-way sensitivity analysis. Although this form of variability estimation is widely used, it may not capture the dynamic relationship between numerous variables in the model. The authors did, however, use two-way sensitivity analyses to capture the relationship between 2 variables that were thought to be highly correlated in the model.

The findings indicated that all four strategies for management had similar effectiveness in the base case with marked differences in cost. The cost of one infliximab dose was assumed to be $2,030 as compared to $17 for metronidazole and $139 for 6-MP. The 6-MP strategy was the least costly, incurring $2,894 for the year, whereas the costs of initial treatment with infliximab followed by 6MP/metronidazole was most costly at $10,112. The strategy employing the combination of 6MP/metronidazole followed by infliximab for treatment failures incurred costs of $6,664. The strategy employing infliximab followed by combination 6MP/metronidazole for treatment failures incurred costs of $10,003. The overall utility values derived from the Markov model were similar between the 4 options, ranging from 0.76-0.77. Given the marked differences in cost and striking similarity in overall utility between the 4 alternatives outlined in this analysis, the incremental cost-utility estimates using the 6-MP alone arm as the comparator were understandably high, ranging from $355,450 to $377,000 per quality-adjusted life-year (QALY) for the other options in the base case. It was found that the decision model results were most sensitive to the probabilities and utilities for improved and persistent fistula health states. Another important variable was the monthly probability estimate for parasthesias associated with the 6-MP/metronidazole therapy. Since there is limited data on the duration of response following infliximab therapy, time to recurrence (or no recurrence) was also tested using sensitivity analysis. The ranges used in the sensitivity analyses seem appropriate and at times are generous. While more emphasis on multivariate sensitivity analyses would have provided helpful insights, the univariate analyses display significantly high incremental cost-utility estimates for management strategies using infliximab.

Overall, this was a reasonably detailed, well done analysis that considered many of the relevant variables involved. Perhaps the major limitation of the analysis, which cannot truly be corrected, was the quality of the effectiveness information given the lack of head-to-head clinical trials comparing strategies using 6MP/metronidazole and infliximab. However, given the best available information, the findings of this evaluation provide reasonable grounds to use 6MP/metronidazole as first-line therapy for the treatment of symptomatic perianal fistula associated with CD, reserving infliximab only for cases that do not adequately respond to 6MP/metronidazole following 3 months of treatment or those that cannot tolerate it.

Glycoprotein IIb/IIIa Inhibitors

Elective coronary stenting is associated with higher rates of periprocedural myocardial infarction than is balloon angioplasty, presumably due to microvascular embolisation of small atherosclerotic material along with platelet thrombus. Abciximab, a glycoprotein IIb/IIIa

inhibitor, has shown superior outcomes at 6-months relative to placebo when administered at the time of stenting. The cost of abciximab is substantial at approximately $535 per dose. Consequently, the costs of this medication need to be balanced against the magnitude of the benefits derived.

The investigators report the clinical and economic results [112] of a 1-year follow-up of a randomized controlled trial (EPISTENT)[113] whose primary intent was to examine clinical endpoints. Consequently, the sample size was based on clinical rather than economic parameters and may not possess power to examine differences in economic endpoints. Three groups were examined in the trial, namely stenting with placebo, stenting with abciximab, and balloon angioplasty with abciximab. In total, 63 centres in both the USA and Canada enrolled patients scheduled to undergo elective or urgent percutaneous coronary revascularisation. All patients received 325 mg aspirin orally at least 2 hours before the procedure and daily thereafter. Ticlopidine 250 mg daily was initiated at the discretion of the investigator before the start of the study agent, if possible, and was given to all patients in the two stent groups. Investigators were blinded to group assignments in this trial. The outcomes of interest in this evaluation were death, myocardial infarction, and repeat revascularisation at 1 year. All of these outcomes were defined as secondary endpoints in the original trial. Follow-up was completed for 99% of all patients enrolled. All analyses were by intention-to-treat. Time-to-event analysis incorporating Cox proportional hazard modeling examined the association between risk factors and survival. Analyses based in such risk factor analysis do not follow the original randomization scheme and may be subject to biases. In particular, diabetes was identified as a risk factor of interest.

Although the stated perspective of the economic evaluation was societal, productivity costs, non-medical costs, and outpatient costs were excluded, rendering the perspective of the analysis to better relate to a third-party payer perspective. Two timeframes were examined in the analysis, namely 1-year and lifetime. The 1-year timeframe may be more easily characterized and perhaps valid whereas the lifetime costs are much more difficult to characterize but may be more relevant. For the 1-year costs, hospital costs were directly collected from the respective hospitals but were calculated from cost-to-charge ratios from hospital bills. Capital costs are typically incorporated into these estimates. Case-report forms were used to quantify follow-up costs to 1 year along with a resource-based linear regression model previously developed from empirical follow-up cost data collected from another trial. Exactly how these two sources were used to calculate costs was not stated. Other data sources were used to quantify costs reported in the case report forms (e.g. Medicare costs were used for physician visits). For the lifetime costs, the Duke Cardiovascular Database was used to extrapolate the 1-year EPISTENT survival results to a lifetime timeframe. No incremental cost differences among the three treatment groups was assumed after the first year. Given this assumption, it may be more reasonable to focus on the findings of the 1-year results rather than those of the lifetime evaluation. The cost-effectiveness parameter was defined as the cost (in 1997 dollars) per life-year gained. Perhaps a more appropriate effectiveness parameter would have been death avoided. An appropriate discount rate of 3% was used, although the authors did not state if both costs and outcomes were discounted. No formal sensitivity analyses were conducted, although the authors do report examining changes in the costs for stents.

Focusing on the two most relevant study groups (i.e. the two stent groups) may be less confusing. The clinical outcomes evaluation at 1-year indicates a statistically significant difference in mortality favoring the stent plus abciximab group (1.0%) over the stent plus placebo group (2.4%) with p=0.037. This p-value is derived from a simple Ch-square test. If a continuity correction is added to the statistical evaluation, the p-value becomes 0.057. Regardless, the absolute risk difference between groups of 1.4% may be clinically meaningful. With respect to myocardial infarction, the risk differences are more striking (i.e. 11.3% for any MI in the stent plus placebo group vs. 5.9% in the stent plus abciximab group). No significant differences were observed with respect to need for revascularization between these two groups. Interestingly, cost data were reported for 60% of patients in both the stent study groups. While the baseline hospital costs in the stent plus abciximab group was relatively higher ($13,228 for stent plus abciximab group vs. $11,923 for stent plus placebo group), the follow-up costs to 1-year were marginally lower ($4,723 for stent plus abciximab group vs. $5,096 for stent plus placebo group). The total costs were therefore slightly higher in the stent plus abciximab group (i.e. $17,951) relative to the stent plus placebo group (i.e. $17,019). While the authors report incremental cost-effectiveness ratios (ICER) for only the lifetime timeframe (i.e. ICER = $6,213 per life-year gained), a simple calculation using the 1-year timeframe and outcomes would lead to ICERs of $66,571 per death avoided (i.e. incremental cost of $932 and an incremental benefit of 1.4% in decreased deaths) and $17,260 per MI avoided in the first year. In the simplest sense, if one assumes no significant 1-year differences in both hospitalization costs (other than abciximab costs) and follow-up costs between groups, the stent plus abciximab ICER for death at 1 year would be approximately $38,000 (i.e. $535 for cost of abciximab assuming a 1.4% overall benefit in mortality) and for MI it would be $9,900 (assuming a 5.4% absolute risk benefit).

The differences between the ICERs at 1-year and lifetime are reasonably large. While ideally the lifetime timeframe should be considered, the need for modeling may significantly decrease the validity of the findings. The ICER for the lifetime timeframe as calculated by the authors is attractive in comparison to other commonly used interventions. Considering cost-effectiveness using a 1-year timeframe may be more reasonable given the nature of the data available. The ICER for the 1-year timeframe, however, is relatively less attractive, although still worth considering for approval.

APPENDIX IX. PROPOSED STRUCTURE AND FUNCTION OF THE CENTRAL PHARMACY AND THERAPEUTICS COMMITTEE

The impetus for establishing a central pharmacy and therapeutics (P&T) committee for the consideration of new and expensive hospital drug therapies comes from the challenge of efficiently and fairly evaluating competing claims on limited health care resources in a population of insured individuals. Few principles have been published to guide the establishment of such a framework. Daniels and Sabin [114] articulate key elements of a fair process of decision-making that require explicit identification of relevant reasons underlying the decisions, establishment of a fair process of appeals to decisions, and procedures for revising decisions. Together, these elements assure 'accountability for reasonableness'. Identifying leadership to champion this issue is crucial to its success. The structure of the proposed process (Figure 14) was based largely on these principles and considered the strengths of three individual drug decision-making bodies, namely CCO (Ontario), DQTC (Ontario), and the Queensland Health system (Australia). This proposed approach should be viewed as an initial attempt at formulating a general structure and should be supplemented and modified by group discussions.

Establishing Leadership

Prior to establishing a central process, it is crucial that a group of individuals be identified as champions to lead this process. Such a leadership should be established as soon as possible. This group must promote awareness and solicit buy-in from all key players involved, especially the key decision-making bodies, namely the OCOTH hospital leadership (i.e. the chairs of the individual PTCs, the directors of pharmacy, and the chief executive officers of each of the hospitals), clinical practitioners, and the MOHLTC. Once buy-in from all relevant parties is achieved, the formal structures can be established and the process initiated. A central administrative 'home' would need to be established in order to coordinate the multiple sources of resources involved in this initiative. Initially, it is recommended that only OCOTH hospitals be involved and all decisions arising from this process should be viewed as recommendations rather than binding decisions. Subsequently, it is recommended that all hospitals in Ontario be a part of this process.

Overview of Proposed Structure

We propose the formation of three primary committees that, as a whole, would be responsible for deciding which drugs warrant a rigorous review process, reviewing the current evidence about the effectiveness and cost-effectiveness of these drugs, making recommendations for approval and developing the indications for drug use, providing a forum for appeals to decisions, communicating these recommendations to relevant groups, and evaluating and monitoring drug utilization following approval.

Figure 14 outlines the basic structure of the proposed central PTC. Initially, the committees may wish to meet a minimum of semi-annually, depending on the volume of drugs to be evaluated in a given year. The following descriptions further outline the process.

Pharmacy and Therapeutics Policy Advisory Committee (PAC)

Objectives

1) To decide which drug therapies with promising clinical utility but potentially large financial burdens should be considered by the Evidence and Economics Evaluation Committee.
2) To review the evaluations provided by the EEC and approve final recommendations for drug approval and conditions for utilization.
3) To coordinate implementation of recommendations/guidelines made by the central PTC with the participating hospitals and funding agencies if applicable.
4) To disseminate findings and recommendations to the participating hospitals, MOH, drug manufacturers, and the public.
5) To coordinate a sound evaluation plan with the Monitoring and Evaluation Committee when a drug is recommended for use.

Composition

This committee will be composed of 10-15 members representing a broad range of expertise, including OCOTH hospital pharmacy members, OCOTH hospital CEOs, practicing clinicians, clinical pharmacists, clinical ethicists, general public representatives, MOH representatives, and policy experts. An executive subgroup of the PAC will be responsible for deciding which drug therapies should be considered through this process. It is recommended that at least 2 practicing clinicians in the therapeutic areas considered be invited on an ad-hoc basis. Furthermore, at least 1 representative from the evidence and economic evaluation committee that considered the drug(s) of interest should be a non-voting member of this committee to provide any clarifications of the evaluation process. Recommendations must achieve majority consensus before they can be considered final.

Time Cycle

At least 4 weeks should be allowed for review of the materials submitted by the EEEC. Materials submitted to the EEEC should also be made available to this committee. Following the meeting, an additional 4 weeks should be allowed for summarizing deliberations and final recommendations. A total of 2 months should be allowed for this process. Initially, the PAC may wish to meet semiannually.

Reimbursement

Members of this committee would receive standard reimbursement rates for their time and expertise. Standard rates used by other groups for similar purposes is about $300 per half-day (see estimated budget section below).

Reporting Structure

The PAC will report to OCOTH. Once all Ontario hospitals have been incorporated into this process, the reporting structure may need to be changed. The PAC will also have working relations with the hospitals, the MOH, drug manufacturers, and the public.

Evidence and Economics Evaluation Committee (EEEC)

Objectives

1) To critically appraise and summarize the available clinical and health economic evidence to estimate expected utilization and formulate cost-effective guidelines for use of the drugs (indications, dosages, etc.). This information will be forwarded to the PAC for final approval. We suggest using or modifying the DQTC guidelines for evaluating the clinical and economic evidence (see appendices).
2) To suggest a preliminary list of clinical and economic endpoints that may be of critical relevance for monitoring purposes.
3) To revisit decisions made by the PAC following drug approval using information provided by the Monitoring and Evaluation Committee.

Composition

This committee will be composed of 4-6 core members and 3-4 ad-hoc members depending on the clinical area being considered. The 4-6 core members should represent a broad range of clinical, methodological, and economic expertise. For example, general clinicians with expertise in critical appraisal, pharmacists, a trained pharmacoeconomist, and a methodologist with expertise in study design and biostatistics may be complemented by ad-hoc gastroenterologists when a gastric medication is being considered. Often the evidence requires external perspectives and sub-specialized expertise. We recommend a roster of clinical and economic reviewers that can be called upon to provide reviews of the available evidence. Depending on the demand, standing subcommittees representing distinct interests (e.g. pediatrics, geriatrics) could also be considered in time as in the Queensland model (see International Overview section). Recommendations must achieve majority consensus before they can be put forward to the Policy Advisory Committee.

Time Cycle

Once the initial request is made, ad-hoc members need to be solicited, external reviewers need to be contacted, and information needs to be gathered from a variety of sources. Following the meeting, the deliberations need to be summarized concisely. This process may take up to 3 months. The EEEC may wish to meet semiannually initially or perhaps more frequently if needed.

Reimbursement

Members of this committee along with the clinical and economic reviewers would receive standard reimbursement rates for their time and expertise. Standard rates would apply.

Reporting Structure

The EEEC will report to the PAC.

Monitoring and Evaluation Committee (MEC)

Objective

To develop and implement appropriate drug utilization and outcomes assessment indicators in OCOTH hospitals to better assess actual drug uptake, financial impacts, and clinical outcomes. This includes designing special access forms for each drug approved outlining key information consistent with the PAC recommendations that need to be faxed or electronically completed. It also includes liaising with individual hospitals to collect the information needed for evaluation.

Composition

This committee will be composed of 7-10 members with reasonably broad representation. Suggested members include OCOTH hospital representatives, clinical pharmacists and physicians, a representative from the EEEC, researchers with expertise in evaluation, pharmacoeconomists, MOH representatives, and representatives from drug manufacturers.

Time Cycle

The development and implementation of methods to evaluate the drug utilization, financial, and clinical outcomes of drug therapy can vary depending on the nature of the drug being considered. The development of the monitoring and evaluation approach may take up to 3 months. Considering that reassessment evaluations will need to be made available to the EEEC and PAC at some point following final recommendations, preliminary reports will need to be completed by this time. It is recommended that a random audit, as in the Queensland model, be conducted to verify appropriate utilization as part of the monitoring and evaluation plan. The activity of this committee and the resources required would largely depend on the decisions of the PAC following reviews of recommendations by the EEEC.

Reimbursement

Members of this committee would receive standard reimbursement rates for their time and expertise. Standard rates would apply.

Reporting Structure

The MEC will report to the PAC and will forward their findings to the EEEC.

Other Considerations

Types of Evidence Considered

To be fair, all available evidence should be considered and left to the discretion of the various committees to evaluate its quality. We recommend that the manufacturer be requested to submit all published and unpublished available documents pertaining to the safety and clinical utility of the drug product along with a budget impact analysis and an economic evaluation of the drug product in comparison to existing alternatives. Such information may facilitate better estimation of the financial impact of the drugs and may provide an opportunity to establish a risk-sharing mechanism that would allow higher-than-projected costs to be paid by the manufacturer. In addition, we recommend that all evidence provided by a drug manufacturer be supplemented

with an independent search for published evidence by a research coordinator dedicated to this process.

Transparency

While transparency of this process should be maximized, certain information submitted by the manufacturer may be proprietary. Discussions among the various committees may bring about confidential issues that drug manufacturers may not wish released to the public forum. Furthermore, a completely open process would allow other competing manufacturers to join in the deliberations. These factors may influence the selection of materials submitted by the drug manufacturer and lead to a biased evaluation of all available evidence. Consequently, standard confidentiality contracts need to be obtained and signed by each participating member. While actual meetings of the various committees may not be open to public participation, a member of the general public is part of the PAC. Regardless, the justifications of decisions of the PAC and the EEEC, stripped of any specific proprietary information, should be made available to the general public for discussion.

Appeals Process

An appeals process to the final recommendations of the PAC should be established. If the PAC requires clarifications of concerns from the drug manufacturer, a period of 6 weeks should be allowed for these clarifications. Similarly, the drug manufacturer or other individuals or groups should be allowed to appeal any recommendations made by the PAC prior to drug utilization.

Overall Time Cycle

Overall, the outlined processes are anticipated to require 6-10 months from the time of request by the PAC to the time special access forms are designed and made available by the MEC. The monitoring and evaluation plan needs to be designed prior to drug utilization to establish the important elements of information that need to be collected. While this timeframe may appear lengthy, judicious evaluation requires time and is crucial to the process. A special access policy may need to be developed to allow patients to receive the drug of interest under relevant circumstances while it is undergoing review.

Other Human Resources and Financial Considerations

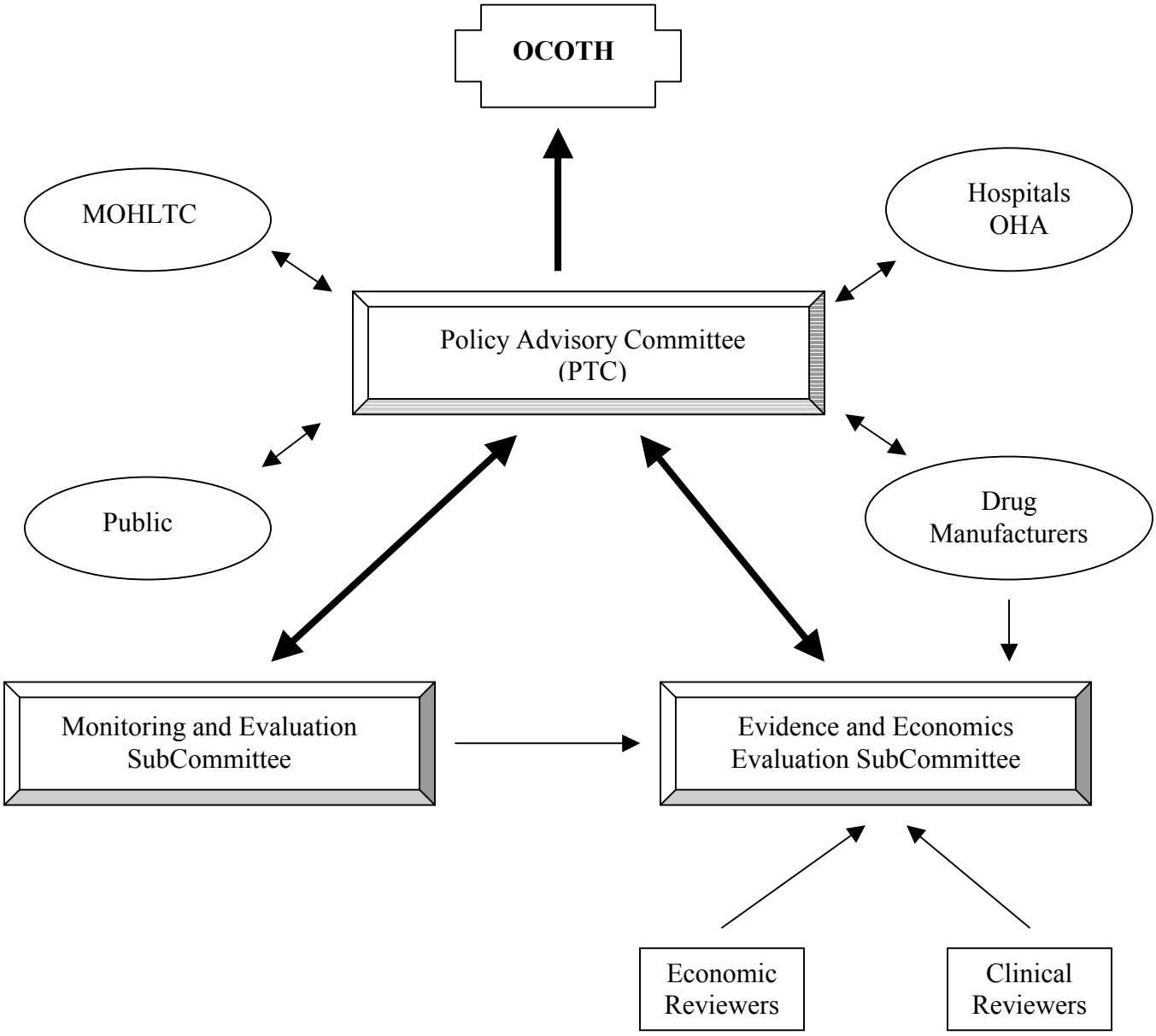
The overall coordination of a central process will require the full time effort of a coordinator. Since an independent search for information in addition to that submitted by the manufacturer is desirable, an individual with some clinical training may be desirable as a committee coordinator. Rather than outsourcing this work, it may be more efficient to include this responsibility as part of the committee coordinator's responsibility. The MEC also requires fairly intensive coordination and may benefit from a dedicated individual with a research background. Finally, some administrative support will also be needed. It is estimated that half-time administrative support will be needed initially.

A rough annual budget for this process is outlined below and is estimated to be approximately $400,000 for one year during which four drug reviews are considered. This estimate does not include costs associated with office space and support systems such as computer stations. Although this figure appears substantial, the amount spent on the drugs themselves will be large.

For example, drugs such as glycoprotein 2b/3a inhibitors alone cost the OCOTH system over $5 million annually in the year 2000. The cost avoidance resulting from such a process (e.g. identifying subgroups of patients in whom use if cost-effective or benefits of risk-sharing strategies) will outweigh these costs. Potential sources of funding include OCOTH hospitals and the MOH.

In the case that central dedicated funds are allocated for a particular drug therapy, a mechanism for distribution would need to be developed. For example, if the MOH agrees to reimburse a particular medication, a mechanism would need to be developed to transfer funds from the MOH to the individual hospitals. This would possibly require further development of information technology to create a distribution system.

Figure 14. Proposed Central Pharmacy and Therapeutics Committee Structure



APPENDIX IX. PROPOSED STRUCTURE AND FUNCTION OF CENTRAL PTC

		Estimated Annual Budget
Fixed Resources		
Committee Coordinator – PharmD level $75 K + 22% benefits	1 FTE	$91,500
Research Coordinator $60 K + 22% benefits	1 FTE	$73,200
Administrative Support $20 K + in-lieu benefits	0.5 FTE	$24,000
		$188,700
Variable Resources (cost per review)		
PAC (12 members) $300/half-day*4 half days per member		$14,400
EEEC (8 members including ad-hoc) $300/half-day * 6 half-days per member		$14,400
Reviewers (2 clinical and 1 economic) $300/half-day * 4 half-days per member		$ 3,600
MEC (8 members) $300/half-day*6 half days per member		$14,400
		$46,800
Miscellaneous		
Telephone		$5,000
Photocopying		$1,000
Couriers		$1,000
Literature Retrieval		$1,000
Travel		$10,000
		$18,000

NOTE: Costs of location and support systems (e.g. computers) and monitoring activities are assumed to be absorbed by OCOTH hospitals

Total Anticipated Costs For 1 Year with 4 Reviews: $393,900

These are estimated costs. Costs will change as evaluations and monitoring functions become more frequent. Funding for this would need to be discussed with OCOTH members and money and time resources from OCOTH facilities would need to be committed.

Institute for Clinical Evaluative Sciences (ICES)
is an independent, non-profit organization,
whose core business is to conduct research
to enhance the effectiveness of health care for Ontarians

Phone (416) 480-4055
Fax (416) 480-6048
Web site: www.ices.on.ca
G1 06, 2075 Bayview Avenue
Toronto, Ontario M4N 3M5
CANADA