A Survey of Pharmacy-Coordinated Investigational Drug Services

Donna M. Cipywnyk and John McBride

ABSTRACT

Over the past few years, pharmacy involvement in investigational drug studies has grown. In 1986, Kingston General Hospital conducted a nation-wide survey assessing the extent of pharmacy involvement in clinical drug trials. The aims of the present survey were to show how Investigational Drug Services (IDS) have changed in recent years, to determine areas that need improvement, and to characterize methods of reimbursement for IDS. A total of 148 Canadian hospitals (300 or more beds) were mailed a detailed IDS questionnaire. A response rate of 68% was achieved. Survey results were grouped in the following categories: increase in clinical trials involvement, IDS staffing levels, sponsorship of trials, major areas of clinical drug research, areas of IDS needing improvement, and reimbursement issues.

The results of this survey indicate that since 1986 pharmacy departments are becoming more involved in the coordination of clinical drug trials. Perceived areas for improvement in IDS were strikingly uniform between institutions, despite a large variation in the extent of existing services. Reimbursement procedures are not consistent and several methods are used to obtain pharmacy funding. Recommendations are offered for assistance in the development or expansion of pharmacy-coordinated IDS in Canadian hospitals.

Key Words: *investigational drug services, reimbursement, research, standards*

RÉSUMÉ

Au cours des quelques dernières années, la participation de la pharmacie dans les études concernant les médicaments en investigation a évolué. En 1986, l'Hôpital Général de Kingston a effectué un sondage à travers le pays afin d'évaluer l'importance de la participation de la pharmacie dans les essais de médicaments cliniques. Ce sondage avait pour buts de démontrer comment les Services de Médicaments en Investigation (SMI) ont changé dans les années récentes, aussi de déterminer les domaines nécessitant une amélioration et de définir les méthodes de remboursement des SDI. Un questionnaire détaillé sur les SMI a été envoyé à 148 hôpitaux canadiens (ayant 300 lits ou plus) et 68% ont répondu. Les résultats du sondage étaient classés en catégories suivantes: participation augmentée dans des essais cliniques, potentiel du personnel des SMI, parrainage des essais, domaines majeurs de la recherche des médicaments cliniques, domaines des SMI nécessitant l'amélioration et problèmes de remboursement.

Les résultats de ce sondage indiquent que depuis 1986 les départements de la pharmacie participent de plus en plus dans la coordination des essais de médicaments cliniques. Il est étonnant de constater que les domaines des SMI nécessitant l'amélioration étaient consistants entre les établissements malgré la grande variation des limites de services existants. Les procédures de remboursements ne sont pas consistantes et plusieurs méthodes sont utilisées afin d'obtenir des fonds pour la pharmacie. Des recommendations sont proposées afin d'assister au développement ou à l'expansion des SMI coordonnés par la pharmacie dans les hôpitaux canadiens.

Mots clés: *normes, services des médicaments en investigation, recherche, remboursement*

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INTRODUCTION

Clinical drug research is an expanding component of our health care system. The steady growth in both the number and scale of clinical drug trials over the past few years can be attributed to a number of factors. Firstly, there has been a gradual recognition that randomized controlled trials are necessary to establish the safety and efficacy of a new drug therapy. It has been estimated that the development of a new drug involves an average of 25 clinical trials and 3000 patients.[1]

Secondly, Canada has not traditionally been fertile ground for clinical testing of new drugs. With the passage of Bill C-22, innovators of newly-approved drugs have seven to ten years of patent protection. This increased marketplace protection is conditional on the research-based pharmaceutical industry meeting certain pricing and investment commitments. These include a doubling of investment in drug research and development as a percentage of sales over a ten year period.

Thirdly, new pharmacological entities are being discovered, pro-

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duced and tested at a faster rate than ever before. Screening methods for active compounds have become more reliable and efficient. The "biotechnology revolution" is having a profound impact on the development and testing of new biologicals in the prevention and treatment of a variety of diseases.

Lastly, the regulatory requirements governing drug products sold in Canada are rigorous and among the most respected worldwide. However, the nature of the regulatory process has resulted in a backlog of drug submissions estimated to exceed 1200 in 1988.[2] The federal government recently established a task force to address the problem of drug review delays. Some of its recommendations are currently being implemented and it is expected that three years will be required to complete the process.[2]

Beginning over ten years ago, the concept of the pharmacy-coordinated Investigational Drug Service (IDS) was established in response to the burgeoning number of investigational new drugs entering the hospital and clinic venues. There has been a general recognition that hospital pharmacists can play a vital role in improving the overall conduct and validity of investigational drug studies. In addition to expanding the traditional task of drug distribution, the IDS concept brings Pharmacy directly into the clinical trials network and assists investigators in all aspects of investigational drug use.

Stolar[3] has identified specific problems arising when there is a lack of Pharmacy involvement in clinical drug studies. These include the following:

1. Poor inventory control resulting in interruptions in drug regimens and delays in initiation of treatment.
2. Drug wastage as a result of improper drug storage.
3. Study drugs being administered to ineligible patients.
4. Incomplete or missing case report forms.
5. Inconsistent patient monitoring.
6. Improper administration of drugs secondary to communication failure.

A logical solution to these problems is the development of a service to coordinate investigational drug studies within the hospital. The pharmacy department is an obvious choice because of its central role and mandate to control drug usage in the institution.[3] The development of a pharmacy-coordinated IDS is an asset to a research-oriented facility.

Both the American Society of Hospital Pharmacists (ASHP) and the Canadian Society of Hospital Pharmacists (CSHP) have established guidelines outlining the responsibilities of an IDS in healthcare facilities.[4,5] The CSHP guidelines are presently being revised.

It is apparent that there is significant variability in IDS functions and development. Large teaching institutions often have advanced services while many smaller community hospitals are involved only with distributive functions. Canadian IDS's have generally followed the U.S. model but with less emphasis on financial considerations.

There is widespread, albeit tacit, agreement that a pharmacy-coordinated IDS is a vital and expanding part of Pharmacy's overall professional services portfolio. As such, there exists a need to accurately characterize the level of IDS development in Canada. Has IDS development kept pace with the growth in clinical drug research? Is there a need to improve IDS staffing or financial reimbursement? If so, how should it be accomplished? What recommendations can be made to help us cope with further increases in clinical drug research?

Objectives

A nation-wide survey of acute-care general hospitals with 300 beds or more was conducted to meet the following objectives: (i) To determine the overall level of investigational drug services (IDS) development in Canada; (ii) To determine how closely current practices follow the revised CSHP guidelines for investigational drug use; (iii) To develop useful guidelines for reimbursement for involvement in investigational drug studies; (iv) To identify areas of IDS that need improvement.

METHODS

The 20 question survey was designed to elicit detailed quantitative and qualitative information about IDS activities across the country. The original IDS survey conducted by KGH[6] in 1986 was used as a model. A request was made in the new version to provide more detailed information about reimbursement methods and policies. In addition, some questions were altered to reflect the revised CSHP guidelines for use of investigational drugs. A one-page "Comments" section at the end of the survey allowed for explanations or opinions regarding IDS practices. Prior to distribution, the survey was reviewed by Dr. J.L. Pater, Director, National Cancer Institute of Canada, Clinical Trials Group, and Chairperson, Department of Community Health and Epidemiology, Queen's University, and Ms. Nancy Paul, Quality Assurance Coordinator, NCIC Clinical Trials Group.

The survey was mailed to Pharmacy directors of all Canadian general or acute-care hospitals with 300 or more beds. The mailing list was compiled using the Canadian Hospital Directory, 1986.[7]

A total of 148 surveys (English language only) were mailed on September 7, 1989. Included in the survey package was a cover letter explaining the nature and goals of the survey, a one-page copy of the results from the 1986 IDS survey[6]

and a self-addressed return envelope. A follow-up letter and an additional copy of the survey were sent to all hospitals that had not returned their surveys after six weeks. Postmarks on the returned envelope were used to identify the survey respondents. December 31, 1989 was set as the final date for accepting returned surveys.

Data from the returned surveys were compiled utilizing a computer database program (dBase IV[R]).

RESULTS

One hundred and one of 148 surveys (68%) were returned after four months. Two of the returned surveys were incomplete, leaving a total of 99 surveys suitable for analysis. Survey response rates varied geographically from a low of 49% in Quebec to a high of 81% in the Western provinces. Of the respondents, 70% (69 of 99) had an established IDS.

With respect to hospital size, 57% of respondents had 300 to 500 beds, 29% had 500 to 800 beds, and 13% had more than 800 beds.

More than 75% of clinical drug studies supported by IDS are conducted in hospitals with greater than 500 beds (Figure 1). However, the proportion of IDS-supported studies in hospitals with 300 to 500 beds has increased from 17% in 1987 to 25% in 1989. For the total survey population, in the past three years there has been a 66% increase in the number of IDS-supported clinical drug studies, from 681 in 1987 to 1024 in 1989.

Of the 96 respondents that indicated their status, 45 were identified as teaching hospitals. Teaching hospitals were responsible for the majority of IDS-supported clinical drug research (92%) (Table I). The proportion of studies supported in non-teaching hospitals rose from five percent (32 studies) in 1987 to seven percent (73 studies) in 1989.

Pharmacy directors were asked to provide the number of full-time positions (FTE's) assigned to their IDS. The average for all respondents was 0.31 FTE (range: 0-1.5). Hospital pharmacies involved in more clinical research had a higher component of IDS staff (Table II). In the majority of hospitals with IDS (61%), all pharmacy staff participated in IDS operation. Other methods of IDS staffing that were described included IDS dedicated pharmacists working singly or in teams on a part-time or a full-time basis.

IDS-supported studies were

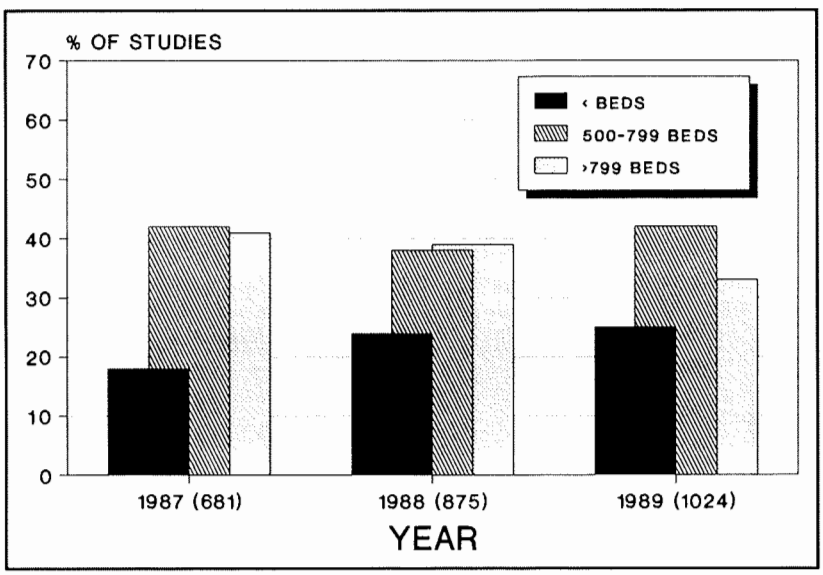

Figure 1: Number of studies completed in responding institutions according to year and hospital bed size. The number in parenthesis next to the year indicates the total number completed in that year.

Table I: Type of Institution

	Number of Hospitals	Studies Sponsored 1987	1988	1989
Teaching	43	616	781	911
Non-Teaching	53	32	54	73
Total	96	648	835	984

Table II: Staffing*

Number of Studies Reported in 1989	Mean # of FTE Allocated	Number of Hospitals
<10	0.05	70
10-19	0.27	9
>19	0.86	20

* Overall mean number of FTE allocated to IDS: 0.31.

categorized according to disease type (Figure 2). Cancer, and infectious disease accounted for 42% of clinical drug research being conducted within the survey population.

Eighty-five percent of respondents knew who sponsored their studies. The major source of funding for IDS-supported research (59%) was the pharmaceutical industry (Figure 3).

The survey assessed how well hospital pharmacists were meeting the basic level of IDS activities as stipulated in the CSHP Standards of Use for Investigational Drugs in Hospitals.[4] Most respondents provided essential services including: policies and procedures for handling investigational drugs (99%), maintain research protocols in pharmacy department (97%), and drug accountability records (91%). IDS activities provided less regularly included: drug information for Nursing (78%), distinct labeling (72%), Pharmacy and Therapeutics Committee review (68%), and statistical summaries more than annually (25%). Verification of informed consent was done by less than half of respondents. Methods of verification included the following: (i) copy of consent form sent to Pharmacy (20%); (ii) verbal confirmation (18%); and (iii) chart review (7%). Forty-one percent of respondents included patient education as an IDS activity in some studies. An additional three percent provided patient education for all IDS-supported trials.

The survey quantified the extent of specialized IDS activities offered (Table III). Some hospital pharmacies had more progressive services and were involved with preparing blinding codes, manuscript writing, patient compliance assessment and data collection and analysis. The special service provided most routinely was ADR reporting (36%).

Pharmacists were asked to identify the areas of IDS that were most

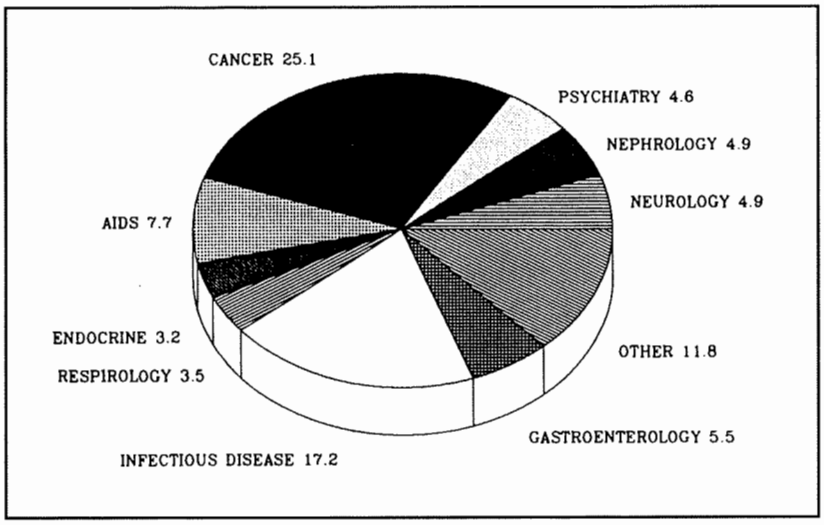

Figure 2: Area of clinical drug trial broken down by disease type.

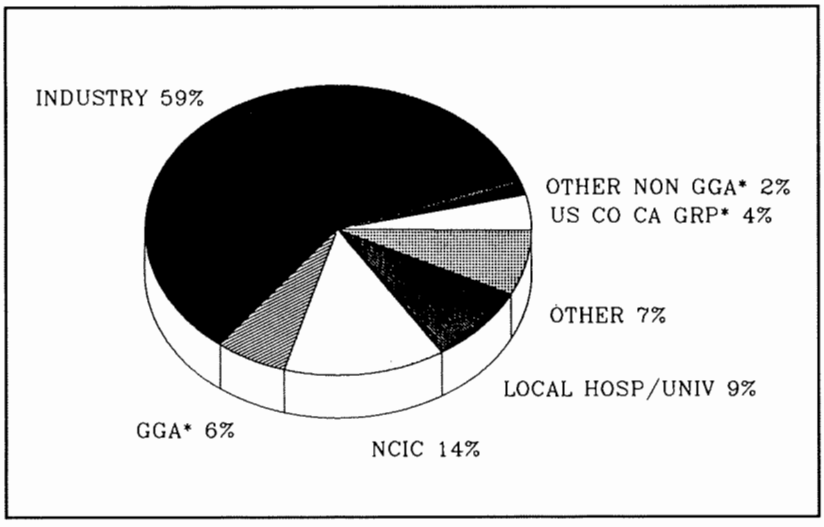

Figure 3: Sources of funding for clinical trials. CGA indicates Government granting agency; US CO CA GRP indicates US co-operative cancer group.

Table III: Specialized Services provided with Investigational Drug Programs

	Percentage		
	Routinely	Infrequently	Never
1. Protocol Development	6	61	33
2. Blinding Codes	23	44	33
3. Data Collection and Analysis	6	58	36
4. Special Dosage Formulation	32	45	23
5. Special Packaging Development	29	42	29
6. Manuscript Writing	3	31	66
7. Co-Investigator	1	37	62
8. Compliance Assessment	17	39	44
9. ADR Reporting	36	50	14
10. Patient Monitoring	18	50	32
11. Patient Education	3	41	56

in need of improvement (Table IV). Monetary considerations (i.e., reimbursement and operational funding), staffing and the overall level of clinical trials involvement were the three most commonly identified areas requiring improvement. Funding of IDS operation was a major concern for many of the hospital pharmacies surveyed. Reimbursement procedures for recovering IDS costs were described as being either inadequate or non-existent. In either case, funds from departmental operating budgets were being utilized to support IDS activities. Many respondents expressed a desire to become more involved in investigational drug trials and expand the scope of their IDS. Most of those surveyed were satisfied with the functioning of their IDS as far as drug disposition was concerned.

Table IV: Program Areas identified as needing improvement

Overall Priority Rank	Percent Ranking High	Percent Ranking Low	Relative Priority
1. Reimbursement	48	7	1.38
2. Staff	35	4	1.30
3. Extent of Involvement	19	4	1.19
4. ADR Reporting	29	13	1.17
5. Coordination and Communication	10	7	1.09
6. Final Disposition and Follow Up	10	16	0.95
7. Drug Handling	3	25	0.76
8. Packaging & Labelling	3	26	0.74
9. Storage	3	34	0.72
10. Drug Accountability	1	34	0.69

DISCUSSION

The growth in the number and scale of clinical drug trials in Canada in recent years has provided pharmacists with an opportunity to become more involved with the clinical trials process. Investigational drug services have become a vital and expanding component of many hospital pharmacies. This nation-wide survey of Canadian hospitals was conducted in an attempt to characterize the level of IDS development in Canada, to identify areas needing improvement, and to develop guidelines for reimbursement for Pharmacy involvement in drug studies.

The response to this survey was very good (68%). The response was highest from the Western provinces (81%) and lowest from Quebec (49%). Lack of a French translation of the survey may have been a contributing factor to the lower response from Quebec.

The total number of pharmacy-coordinated studies has increased from 648 in 1987 to 984 in 1989 (66%). This significant increase may reflect changes in the Patent Act, recent advances in biotechnology, and the stringency of Canada's regulatory approval process.

Compared to 53% in 1986[6], 59% of all IDS-supported clinical trials in 1989 were sponsored by the pharmaceutical industry. This slight increase could be an indication that research-based companies are beginning to fulfill their commitment to increased investment in Canadian research.

Although differences in clinical involvement are expected based on the size of the service and extent of Pharmacy participation in research, the presence of the basic IDS services should be uniform. The Canadian Society of Hospital Pharmacists has recently revised the Standards of Use for Investigational Drugs in Hospitals. These standards do not address the IDS concept *per se;* however, they outline all of the responsibilities of a modern IDS and emphasize the need for Pharmacy involvement. When the survey was conducted, these updated standards had not yet been distributed. Review of the guidelines should increase awareness and institution of the basic services that an IDS might provide.

Some of the weakest areas of IDS performance today are chronic problems that are not easily remedied. The three greatest concerns of IDS pharmacists in 1989 were: i) monetary considerations; ii) manpower; and iii) extent of involvement in clinical trials. These have remained essentially unchanged from the problems identified by the 1986 survey[6].

Hospital pharmacies are often forced to draw upon their already strained budgets and staff to meet the demands of IDS operation. Adequate reimbursement for services provided would help to alleviate this problem. Only 44% of the survey respondents had reimbursement policies and the average pharmacy cost per trial ranged by as much as 30 fold between institutions. Many charge only a dispensing fee, while others have itemized cost-finders which justify their fees and help the IDS to be self-supporting. These cost-finders also assist investigators in developing budgets for clinical trials. Reimbursement should be based on personnel and materials costs associated with providing the required services for a particular study. The aim of a billing scheme would be to recover the costs of providing the service. Costs should be kept as low as possible to make IDS affordable for sponsors and encourage its use.

Lack of personnel is another problem facing IDS. The average number of full-time equivalents allocatd to IDS in the survey population was 0.31. One contributing factor to the staff problem is the lack of money to fund IDS positions. This may be corrected by improvement of reimbursement

procedures, leading towards a self-supporting IDS. It would also be useful to measure IDS workload to justify IDS staffing in the Pharmacy budget. It is difficult to attract staff to an IDS in institutions where the IDS pharmacist is performing essentially technical tasks. This may be remedied by dividing tasks between pharmacists and pharmacy technicians. Pharmacists should ideally be involved with trial set-up and other administrative or clinical tasks. Technicians should be responsible for drug distribution and for IDS inventory control and record keeping. As well, details of billing, other than the initial assessment, do not require a pharmacist's involvement.

Recommendations

Based on the results of this survey of investigational drug services in Canada, the following recommendations are offered:

1. The new CSHP Standards of Use for Investigational Drugs in Hospitals should be reviewed by hospitals currently handling or planning to be involved with investigational drugs. Policies to meet the standards should be established.

2. Pharmacy departments should actively promote IDS as an integral part of their clinical and distributive services. IDS staffing should be included in the regular staffing pattern of each Pharmacy department, including both pharmacists and technicians. Workload measurement of IDS functions is an essential part of this process.

3. In order that research pharmacists collectively discuss their concerns about reimbursement, quality assurance, staffing levels, and other common problems and goals, CSHP should consider establishing an IDS professional specialty group (PSG).

4. Development of clinical IDS activities such as patient monitoring, counselling, protocol development and manuscript writing should be encouraged after basic services are established.

5. The issue of reimbursement for IDS should be addressed by all Pharmacy departments offering IDS. The most practical way to bill sponsors for studies is based on projected personnel and material costs to coordinate a study. Personnel costs should be based on both the time required for each specialized task and the person who performs the task (i.e., pharmacist or technician). After reviewing the protocol, the pharmacy functions and fees should be discussed with the investigator(s). Table V provides a useful "IDS cost-finder" guide for estimating labour and materials for a given Investigation Drug Trial.

CONCLUSION

The future of IDS is largely dependent upon the ability of pharmacists and investigators to share in the planning and execution of clinical drug trials. Hospital pharmacies should not be discouraging participation in meaningful and ethical drug research by demanding reimbursement fees that are beyond the means of sponsors. Likewise, investigators and sponsors must be aware of the need for reimbursement of IDS costs. Ideally, IDS expenditures could be recovered completely thereby reducing the financial and staffing stresses on the pharmacy department. This ideal requires careful evaluation of current IDS workload and development of a corresponding annual budget. Support for IDS operation must be approved by hospital administration. Setting fees for individual trials requires detailed knowledge of the type and extent of pharmacy involvement.

Table V: IDS Cost-Finder

A. *Administration Fees:*
- — set-up of Pharmacy procedures*
- — preparation of drug data sheets*
- — randomization code preparation*
- — in-services (nursing/pharmacy)*

B. *Medication Fees:*
- — cost of drug
- — cost of dispensing supplies
- — costs in maintaining inventory and drug handling (overhead)**
- — labor cost for preparation and dispensing of drug**

C. *Subject Fees:*
- — record keeping**
- — patient counselling*
- — patient monitoring*

D. *Other Fees:*
- — Call-back fee*
- — Special services*
  - e.g. — protocol development
  - — collection/analysis of data
  - — manuscript writing
  - — compliance assessment

* Pharmacist completed task
** Pharmacy Technician completed task

For references see page 200

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