House of Commons
CANADA

Standing Committee on Health

HESA • NUMBER 019 • 2nd SESSION • 39th PARLIAMENT

EVIDENCE

Tuesday, April 1, 2008

Chair

Mrs. Joy Smith

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● (1105)

[*English*]

The Chair (Mrs. Joy Smith (Kildonan—St. Paul, CPC)): Good morning, and welcome back from the break. It's so good to see everybody here.

Committee business has started up, and we're really pleased to have our guests here today. But before we hear from our witnesses I would like to ask members of the committee to devote a few minutes at the end of today's meeting for consideration of committee business and the proposed meeting schedule. You will get that schedule following the witnesses' presentations this morning.

Madame Gagnon.

[*Translation*]

Ms. Christiane Gagnon (Québec, BQ): I would like you to set aside some time to discuss certain points, because I will not be able to stay longer than an hour.

[*English*]

The Chair: Excuse me?

[*Translation*]

Ms. Christiane Gagnon: I will have to leave after an hour. So if there is a vote on a proposed work plan, we should set aside some time to discuss it.

[*English*]

The Chair: Mr. Tilson.

Mr. David Tilson (Dufferin—Caledon, CPC): We all have difficulties with our schedules. If we are finished with our guests I have no problem with that, but if our guests are still here I think it would be most inappropriate to delay our guests simply for one member who's unavailable.

I appreciate that we all have those difficulties, but we've invited our guests to come here, and they have priority.

The Chair: Mr. Fletcher.

Mr. Steven Fletcher (Charleswood—St. James—Assiniboia, CPC): Obviously the Bloc members are an important part of the committee. I wonder if we could move the future business to the next meeting where they could contribute.

The Chair: I would like to present this to you. Our next meeting will be rather full, with little time. Today we have two witnesses, and if we get through the presentations and the questions and answers, we could get the business done a little earlier. But it's the will of the committee.

I'll go over the situation for some of the members. I said that at the end of the meeting today we have some committee business to do. We have two witnesses and we don't want to curtail their time or the questioning, because they have some very important things to share with us. Madame Gagnon has to leave early, and asked for the committee business to be dealt with earlier. At that point two members said we have to make sure we don't short-change the witnesses; we need to hear everything they have to tell us. Mr. Fletcher suggested we leave the committee business until another day.

If the witnesses are finished and the questioning is finished within the hour or so, should we go straight to committee business? Is everyone willing to do that?

Mr. Tilson.

Mr. David Tilson: I don't know how much business it's going to entail. The guests today have had no notice that they might be short-changed. The guests next week could be given notice that the regular meeting will end at a certain time.

We're killing all kinds of time right now blathering about this. My suggestion is that we put this business on for next week so Madame Gagnon will have an opportunity to participate in the business meeting. The guests next week can be put on notice.

The Chair: Is everyone willing to have committee business next week?

Some hon. members: Agreed.

The Chair: We will do that.

I would like to welcome today Ms. Madeline Boscoe, executive director of the Canadian Women's Health Network; and Dr. Bruce Carleton, senior clinician scientist from the University of British Columbia, Child and Family Research Institute, B.C. Children's Hospital.

I'd like to remind witnesses that you have ten minutes each to make your presentations. Following that we will have questions from all the committee members.

Ms. Boscoe, I would ask you to begin.

Ms. Madeline Boscoe (Executive Director, Canadian Women's Health Network): I'm delighted to do that, and thank you very much for the opportunity to come today.

It's also great to see the number of Manitobans on this committee. I guess it says something about how seriously we take this aspect of Canadian culture.

An hon. member: Hear, hear!

Ms. Madeline Boscoe: I was going to bring a Jeannnie's cake, but just couldn't get it together. I'm sorry.

The Chair: We have to send you back for one, Ms. Boscoe.

Ms. Madeline Boscoe: Okay.

It might be helpful for you to know that I am a nurse by training. I work at a community health centre for women in Manitoba, where for 25 years we've been dealing with the issues of drug and device safety, including tracking women with diethylstilbestrol or DES exposure for screening, raising questions about the relative value and potential harm of hormone replacement therapy, the impact of reproductive technologies on the lives and bodies of women, and other issues around drug regulation.

Currently we are working on a team developing sex- and gender-based analysis tools for systematic review, hoping to improve our knowledge base for decision-making, and we are involved in the development of the proposed drug effectiveness research network, which I believe you are aware of.

The CWHN is a national network working to improve the lives of women and girls in Canada by undertaking research synthesis and collecting and distributing information. We are in fact a knowledge broker.

I am lucky enough to have participated in the consultations Health Canada has had on their proposed progressive licensing regime and the life cycle approach. This is laudable and demonstrates that Health Canada is finally moving to update its regulatory infrastructure.

The department I think also should be congratulated on its increased efforts to engage the public and community groups in its processes and deliberations. The establishment of the Office of Consumer and Public Involvement is an excellent example.

I also particularly wanted to take this time to thank the government for its rigorous defence in the CanWest Global charter challenge to the existing direct-to-consumer advertising regulations. Although we, like other groups, feel strongly that there's more to be done in this area, we are delighted and grateful for your active work in this area. Preventing direct-to-consumer advertising is directly related to keeping manageable and fundable medicare.

Given the rich testimony before you, though, I don't want to repeat what's already been said but want more to say that we absolutely support the recommendations and observations made to you by PharmaWatch, the Canadian Medical Association, the Canadian Health Coalition, Women in Health Protection, and Drug Safety Canada. My remarks are to enhance those areas.

Firstly, post-marketing surveillance is increasingly important to women, and of particular interest because the implementation of our commitments to sex and gender analysis in health research and the evaluation of health products is still not yet routine.

For example, in the United States eight of ten prescription medicines that were withdrawn from the market between 1997 and the year 2000 caused more adverse effects in women than in men, and they found that only 22 participants in the clinical trials were in fact women. This lack of subgroup analysis by sex leads to potential for error and for harm at the regulatory area and at the practice area. That's improving. Post-marketing processes are critical building blocks for women and for men. I would also suggest that you always include the term vaccines in your deliberations.

However, this must be a transparent process, not one managed by the industry. Like the move to the public reporting of clinical trials and clinical trial results, post-market surveillance, including adverse reaction reporting, must be publicly managed and publicly accessible. We also need to be including the existing products that are on the market, not just new products. This is really important because of the level of evidence for the evaluation of these products.

As you identified in your report “Opening the Medicine Cabinet”—one of my favourite documents of all time—increasing the capacity of Health Canada, and I would add of other infrastructures, is going to be absolutely essential. People cannot do this on the side of their desks. This includes supporting the proposed drug research and effectiveness network and expanding the work of CADTH, the Canadian Agency for Drugs and Technologies in Health. As well, as you have heard, there is an important and critical role for patients in adverse drug reporting and post-marketing surveillance, and infrastructure for outreach to them is needed.

However, improving post-marketing surveillance is only one component. I am, however, extremely fearful and worried that strengthening post-market surveillance will be used as an excuse, if not a smokescreen, for lowering the standard of evidence for the requirements of new health products.

● (1110)

There are already many problems for women, children, and the elderly. I would suggest that the current standards for the approval of a drug need to be nuanced and made more robust. We need products to be tested on the populations that are actually going to be using them. I know it sounds like a radical thought, but there you go. We need a framework, one that recognizes that standards for safety and effectiveness need to be different, depending on the goal of the product. Products that large numbers of Canadians use for prevention, such as hormone replacement therapy for women, or statins, need a different order of evidence from those used in life-threatening conditions. Drugs used by the elderly and Canadians who use multiple drugs need to be tested on those populations before they come on the market. If Canadians are going to be research subjects, I believe we have an ethical duty to tell them so.

As we evaluate drugs, we think it is important to include at the outset information about head-to-head trials and real-world effectiveness. We don't want to be doing this at the end. Developing a process for researchers, consumers, and citizen engagement in the approval of clinical trials, and in the anticipated pre-application consultations that will be put in place before a formal notice of compliance, would be a way to go.

We recognize that there are huge pressures on you as parliamentarians for drugs to be approved faster. Everybody lives that reality. However, I think there is now some evidence that the time requirements placed on Canadian and American reviewers is creating harm. A recent study has shown that safety problems in new drugs are very much tied to the timelines for their approval. I have the details of this study, but I won't take time to explain them now.

My next point is one that probably is predictable. It is improving the management of health products, incorporating sex and gender analyses into the regulations and legislation that you will be working on. Sex and gender are not just intellectual concepts at this point. We now know that sex and gender matter in ways involving the basic science, the basic genetic level. They manifest in many, many different ways. The pharmacokinetics and the pharmacodynamics of drugs are important. Examples include the effect of the menstrual cycle on the metabolism and use of drugs, and the way in which genetic expression and sex are linked. For example, for some reason, boys are particularly vulnerable to risks for cancer, asthma, birth defects, and learning and behaviour disorders. Women seem to have an increased risk of immune disorders and a higher risk of gene immune suppression disorders than men. We're at the very early stages of understanding this.

We also know there are big differences in the way in which women and men experience health services and health utilization. I won't reprint the front page articles from *The Globe and Mail* on the experiences of women and men when seeking hip replacement surgery.

We are learning more, but we have a long way to go. I think it is critical, and I would beg you to actively consider enshrining into legislation and regulation a policy that requires a sex and gender analysis in all aspects of the drug review and management process. The United States has moved to do so. Here in Canada we've made some good steps. We've had a guideline for almost a decade. But guidelines are only guidelines and the real money is in the regulation and the legislation.

I'm hoping we can talk a little bit more about that.

How am I doing for time?

● (1115)

The Chair: You have only about ten seconds left.

Ms. Madeline Boscoe: I would say that my written remarks to you are going to deal a little more with lifestyle management and the whole concept of health information and access. As you may know, Madam Chair and members, I co-chaired the Minister of Health's advisory committee on the health info highway and consumer and public health information. I have some remarks on that.

The Chair: Thank you, Ms. Boscoe.

Dr. Carleton, could you give us your presentation please?

Dr. Bruce Carleton (Senior Clinician Scientist, Child and Family Research Institute, B.C. Children's Hospital, University of British Columbia): Good morning, Madam Chair and committee members. I'm a clinician at the Children's Hospital in Vancouver, and I would like to speak to you today about post-market surveillance from the standpoint of somebody who works daily with patients in the Canadian health care system, and about what I think can be done about this system to make it even better.

Adverse drug reactions are a major cause of morbidity and mortality in this country and other countries around the world. Adverse drug reactions or drug side effects are the fifth leading cause of death in North America. If it were up to me, I would ban the term “side effects” from the lexicon and change it completely to “adverse drug reactions”.

We need to understand the fact that this is a major public health issue, and we need to address it. The difficulties, however, are that idiosyncratic response—the response that one person has to a drug that is an effective remedy for a particular ailment when for another it's actually harmful—make it very difficult to factor into regulatory change these kinds of issues.

We have a post-market surveillance system in this country. Most countries around the world do. Some are mandatory, some are voluntary. In either case, mandatory or voluntary, they predominantly don't work. In Canada, 95% of adverse drug reactions are never reported to regulators. Again, making it mandatory won't change that number—95% incomplete—significantly.

What we need is a system that's directed at solutions, at solving adverse drug reactions, not just at collecting reports. We need a solution-directed approach, and unfortunately with so few reports coming in and those that come in actually being incomplete, not having sufficient detail, it is very difficult to analyze the reports and to come up with meaningful solutions to these safety problems.

As an academic, I can tell you that one of the key examples of this is the methodology. You don't just collect reports of adverse drug reactions. You have to collect reports of people who took the drug and didn't have an adverse reaction so you can compare the two. That's not done. That's part of the problem.

What's the solution? One possible solution is to look at human genetics and the role it plays in drug biotransformation. Drugs are transformed in the body. They are not just consumed and then eliminated as the same product that you took by mouth, or took intravenously, or injected another way. Drugs are transformed, and in these transformations there is a variety of many steps for most drugs. Each of these steps is controlled by genes. Some of these genes are expressed when you are a young child, and some are expressed later in adulthood, which means that for children, an age-based approach, bearing in mind Madeline's comments about gender as well, is also important.

Pharmacogenomics can help by looking at how genes control the biotransformation of drugs, and whether some of those biotransformation products are toxic or not.

About four years ago, Michael Hayden, a geneticist in Vancouver, and I began a $10 million study to look at the genetic basis of drug reactions in children. To date we have more than 9,000 cases from Canada and controls from Halifax to Vancouver that we've captured with our surveillance network. We built a post-marketing surveillance system that could allow us to do the work that we wanted to do, since we didn't have one in Canada that we could use.

That system has proven remarkably effective. It has 13 paid clinicians, whom I pay, from across the country from Halifax to Vancouver at all the children's hospitals that are the tertiary referral centres. We have Halifax, Sainte-Justine in Quebec, the Hospital for Sick Children in Toronto, etc. There are eight sites. We're adding nine additional sites this year.

The goal is to find cases of adverse drug reactions, to find matched patients who haven't had adverse drug reactions but who took the drug, and to look at the genetic differences between them. I can report from this work today that we have found the genetic basis, we believe, according to preliminary data, for three serious and fatal drug reactions, and we will be on the quest for many more in the coming years.

I wanted to tell you a little bit about what we've discovered, and then also provide some forward thinking on where we are going to go next. The first report I wanted to tell you about was codeine.

● (1120)

Tylenol 3 is an over-the-counter non-prescription pain reliever that is very effective. Tylenol 3 actually has codeine in it. Codeine is a weak narcotic. When it is biotransformed in the body, it becomes morphine, which of course is a much stronger narcotic. We discovered a case of a child who died, presumably of sudden infant death syndrome, in Ontario about two years ago. We reported this case in *The Lancet*, the British medical journal.

In this case the child was found dead of presumed sudden infant death syndrome. This is a diagnosis of exclusion, meaning that if there isn't any other reason for the child's death, that would be the diagnosis. A follow-up toxicology screen by the Ontario coroner revealed that this child actually had lethal levels of morphine in the bloodstream. How does a 13-day-old child get morphine in the bloodstream? There was no apparent reason for that.

We analyzed the breast milk of the mother and found twenty times the level of morphine that one would expect in her breast milk. The reason is actually genetic. It was basically two gene variants that she possessed that caused the death of this child through breastfeeding, one of the worst possible events that I can imagine for a patient.

These genes are actually fairly common variants. If you've ever taken Tylenol 3 or you know people who have, you know that there are big differences between how people respond. Some people say that if they take one of those tablets, it knocks them out cold; some people say that if they take two or three of those—that would be me—they don't feel anything different.

These are genetic differences. This mother had this kind of response. She actually had constipation and somnolence. She was very, very tired from this medication. Those effects are well-known opiate effects from drugs like morphine and codeine. She went to her physician; the dose was reduced by half, and it still killed her baby.

This a major issue. What we've now come up with is a way to predict in whom these reactions are likely to occur and thus to avoid using the drugs in those patients, or at least to use them in much, much smaller doses.

That's one example of where we're heading.

We've done some follow-up work with Motherisk, the pregnancy and breastfeeding information line in Canada, with women who have called about codeine, and we're publishing those results, we hope, in the coming months. We've submitted them for publication.

The next reaction I want to talk about is cisplatin. Cisplatin is the drug of choice for ovarian cancer and many solid tumours in children and adults. It's a very effective anti-cancer agent. It's been around since the 1950s. It has an 80% to 85% success rate in inducing remission or cure.

Unfortunately, it causes deafness. In pediatrics this is well understood and well accepted. In adults, it isn't even monitored. I believe that it is a problem in adults as well as a problem in children. I want the effective outcomes, and I think hearing is a reasonable sacrifice for life, but I would really like to save people's lives without any loss of hearing and without causing another problem.

We've begun a quest to find out if there's a genetic difference. We've found a gene that is 100% predictive of severe deafness, deafness at the level at which a cochlear implant or hearing aid needs to be placed. This relationship is very strong.

Cardiovascular disease and cholesterol are linked. We all know that. We've been told this many times. The link is an odds ratio, a statistical calculation of about 1.7. In the case of cisplatin and deafness, the gene that we found is an odds ratio of infinity, because it is 100% predictive: it only occurs in people with severe hearing loss. It doesn't occur in anybody else. An odds ratio of infinity is quite substantially greater, obviously, than even the link between cardiovascular disease and cholesterol.

The third reaction I want to talk to you about is anthracyclines. Anthracyclines are the drugs of choice for leukemias and many other cancers. They are used as extra drugs for many types of cancer treatment. In the anthracyclines doxorubicin, daunorubicin, and epirubicin are many names of these drugs in this chemical class. They are very effective—in 80% to 85% of cases, they induce remission or cure—but again they have a limiting toxicity. That's cardiotoxicity, heart toxicity. About 3% of the children we treat at B. C. Children's Hospital end up dying of their cardiovascular complications from their anti-cancer drug. About 8% of our children end up on the cardiac transplant list in British Columbia.

● (1125)

There is a 61% mortality rate for this particular reaction. Again, we found the gene for this particular reaction. It's a membrane transporter that's responsible for removing anthracyclines from the cardiac cell. In the cardiac cell, once the drug gets in there it can't get back out and causes cell death. That's the mechanism we believe is responsible.

Again, these are preliminary results with a very high odds ratio of about 20, meaning you would be 20 times more likely to have cardiotoxicity if you had this particular gene than if you didn't. These are very significant findings and show that when you combine clinical pharmacology and the biotransformation of drugs with human genetic profiles, you can actually predict in whom reactions are likely to occur. And that's where we are heading, predictive testing.

The last thing I wanted to say is that we need many more of these kinds of predictive tests. I think Canada can actually lead the world. I've spent 20 years of my life studying post-market surveillance and running systems in two different countries to try to improve the quality of what we're doing. I can actually do a post-market surveillance system finding the genes, as I've described to you, for about $1.5 million a year. This is not an expensive process. This is about getting the right people engaged and the right attitudes in place to actually make a difference.

What this has enabled me to do is to get other clinicians involved. When you show people that reporting so we can have a solution makes a difference, they'll report, they'll participate. They don't want to see regulation for the purpose of regulation. It's great to talk about improving safety of drugs for Canadians, but we need solutions not just great frameworks.

Lastly, I'd like to say that it's like building a car. Start with a Kia, not a Cadillac. Start with something a little less impressive perhaps than what you ultimately want to create in terms of a post-market surveillance system. I would suggest drug-safety-focused, solution-directed. Pick one drug you want to find a solution to, or two or five, but just a few, and move from there.

Thank you.

● (1130)

The Chair: Thank you so much.

If you permit me, committee, I'd like to ask one question before we start the committee.

I'm very interested in this heart drug. As you know, cancer patients who have very heavy chemotherapy are given a drug that could affect the heart quite adversely and that belongs to this family. How do you know? Right now what you're saying is that in Canada they don't test for this gene in the body.

In other words, what you're saying as a scientist is that even if the patient is forewarned, you could predict as a scientist whether or not the heart would be affected if we did that test. Is that correct?

Dr. Bruce Carleton: That's right, but we're the first to sort of couple these things together, and the results are preliminary. As you know, the best work that's done by scientists is that which is peer reviewed. We should get this published, and then we should move this into the commercial market.

Michael Hayden, the geneticist, and I were just awarded a commercialization grant from Genome British Columbia. We plan on bringing one of those three discoveries to the commercial market. I'm particularly interested in doing that quickly, for a couple of reasons. It's mostly because it can help to further endow the work we're doing. Doing this kind of work and getting the kinds of funds you need to run a national surveillance system is very difficult for an academic, and it requires continuous care and feeding. At the end of my three-year funding stint, which ends in December, I will have no funding. People begin leaving surveillance positions six to eight months before the funding runs out, to find other positions. It's critical that we endow this work so that we can continue to make it grow.

The Chair: Thank you, Dr. Carleton.

Ms. Kadis.

Mrs. Susan Kadis (Thornhill, Lib.): Thank you, Madam Chair.

Welcome to our guests.

I found the statistic particularly disturbing that eight out of ten people in the United States had experienced adverse drug reactions. I want to clarify. Was it eight out of ten people in the United States, or that eight of ten were women who experienced adverse drug reactions?

Ms. Madeline Boscoe: Eight out of the ten prescription medications that were withdrawn from the market between 1997 and 2000 caused adverse events in women...than in men. When they went deeper into that, it turned out that part of the reason was that only 22% of the participants in the trial were women.

Mrs. Susan Kadis: Along those lines, is there a difference between how women's drugs are treated as opposed to men's drugs? You seemed to imply in your presentation that there was a difference, but I wanted to confirm that.

Consider, just as an example, the HPV vaccine. Are we sufficiently cautious about the long-term implications? What resources are being put into studying the long-term effects?

● (1135)

Ms. Madeline Boscoe: As you may know, vaccine and drug approval processes in Canada right now are private except for very extraordinary circumstances, so I can't really comment on what happened internally in the department. However, as you may know, my agency has been involved in thinking about the issues of vaccines and long-term safety.

I must say that the data do not suggest that this vaccine is any more biologically, physiologically unsafe. The questions we were raising around the HPV vaccine really were about added value and cost-effectiveness, given the low amounts of cervical cancer that are in the country and given the fact that the women who do die from cervical cancer die from lack of care, not from their disease.

Mrs. Susan Kadis: You mentioned that drugs ideally should be tested on those who will be utilizing them. I think we would all agree on that. In the case of HPV in particular, as we understand it from our best information, young children were not tested but were recommended to be given the vaccine.

Would that be an example?

Ms. Madeline Boscoe: Yes, that would be an example from my perspective. Also, young boys were not included in those trials either.

Mrs. Susan Kadis: From a woman's perspective, what could be done to improve post-market surveillance, in your opinion?

Ms. Madeline Boscoe: I did spend a bit of time on the garbage-in, garbage-out issue. I actually feel strongly that what we need to be doing is looking at sex and gender at the beginning of the process—that is, what's going on in the clinical trials, what's the notice, what's the review, what's the notice of compliance? And because we're not, I think we need to make sure, as we engage citizens in post-market reviews and contributions through adverse events reporting, that we do some special outreach to women.

That being said, the fact is that if we look at who makes up health care providers, if we look at who makes up unpaid health care providers in families, it's women. Inevitably, then, whether we like it or not, we're going to be doing a lot of this reporting anyway.

An educational campaign and a skills campaign for the Canadian public to engage in so that they understand the differences and the symptoms—that's part of the process. It's tied into the quality of health information that patients get when they're given these drugs. They're often not told that they have a drug that's maybe had 5,000 people in it, or told any of those specific things that would make the consumer sit up, take note, and say, "Well, gee, that doesn't sound like me; I'd better be very careful."

Doctors don't have the time, and there are very few materials I would trust right now, to provide what I would call the "decision support" tools that are needed. Hence, part of post-market surveillance is really about a health information system in a very different way.

Mrs. Susan Kadis: I may be wrong, but it seems to me that a lot of the issues with post-market surveillance, from your perspective, could be addressed, probably from both perspectives, at the earlier stage. In other words, the post-market surveillance part of that process is actually going to be solving problems and difficulties that could have been dealt with at an earlier stage.

Ms. Madeline Boscoe: Yes, we need to do it at the front end, but also we need to understand that things will creep up. Rare reactions will creep up.

The other reality is that because we don't require head-to-head—that is, comparisons between drugs and interventions—before we approve a drug, the other thing post-market surveillance does is tell us whether or not the product really works. I know it sounds silly even to say that, but we need to realize that taking something that doesn't work, for whatever reason you were given it, is not just an adverse event; it's an incredible waste of money, time, and resources.

Mrs. Susan Kadis: To our other guest, what do you believe should be done as far as post-market surveillance from the perspective of children?

Dr. Bruce Carleton: Children, like women, are somewhat disenfranchised from the system for the same good reason initially: to avoid testing drugs on children, women, and unborn children is probably a good ethical boundary to adhere to at some point. Unfortunately, that means these populations are largely untested when drugs enter the marketplace.

I don't believe we can determine drug effectiveness and safety without post-market surveillance. It can't happen earlier. Clinical trials give us an idea of where drugs can be used safely and effectively, but actual use in large, diverse populations gives us our true understanding of where they're most valuable.

For children, it's equally important that we understand the scientific determinants of drug response. The difficulty in all of the discussions we're having this morning is heterogenity of response. For every one person who doesn't respond to a therapy there are three who do, and vice versa. For every five who respond well there's one who has a serious and permanently disabling adverse reaction. It may be fewer than one; I'm not using actual numbers here. I'm just suggesting there is wide variability. At the clinical level, we're constantly faced with what's going to work, what can we try, and what would be best to use.

● (1140)

The Chair: Thank you, Dr. Carleton.

Madame Gagnon.

[*Translation*]

Ms. Christiane Gagnon: Thank you.

Good morning, Ms. Boscoe and Mr. Carleton. We are happy that you are here today. You have raised an important issue about the number of women and children participating in clinical trials.

I would like to talk about a vaccine that has caused a number of deaths. I am referring to Gardasil, which is used for the human papilloma virus. To date, it has caused 11 deaths in Europe and in the United States.

I would like to hear your views on this situation. How do you think Canada can be more proactive in providing the public with information? You are undoubtedly aware of what happened, are you not? Did the parents receive any information? Very few girls between the ages of nine and 15 participated in the clinical trials. Apparently, there were 1,200 girls, compared to 20,000 women from the female population in general. What would you like to see? We hear that there have been deaths and serious consequences. It is more than an adverse effect when people die, it is the limit of what is acceptable. How can a government be more proactive with respect to tragic situations like death?

[*English*]

Ms. Madeline Boscoe: That's an excellent question, and I think it's one of the reasons why I suggested that we keep vaccines in the drug and health product field. Right now they run in a separate.... They come from a separate history in medicine, and because we are now using them so much more regularly.... The last time it was hypertension, and the report before that was one on nicotine, a vaccine for smokers. So we're going to see a lot more of these kinds of products come on the market, and I think we are going to need to develop different frameworks.

I would say that in the past, as with any other pediatric drug, it's not been unusual as common practice for drugs, devices, and vaccines to be studied on one population and then used on another. The ethics involved here were particularly, to be honest, because of the unique nature of what they were doing. They were testing for HPV in vaginas, and to do that on young girls is problematic. So I am very sympathetic to the struggles ethically.

This vaccine does look like it could be a fabulous thing. Our position at Women's Health Network is that we would have preferred to have seen more research, better modelling. We don't, for example, really know the prevalence of the HPV vaccines that have caused harm in our backyard. In the backyard I'm in, it doesn't look like 16 and 18 are the big majority that they are in other countries. That's very important if we're going to start telling people that they're protected from something when they're not.

We're also very concerned that we know only that this vaccine lasts for about six years. It's been in clinical trials for only six years. If we look to our experience with chickenpox and mumps, we know the vaccines wear off. This is extremely worrying for those of us in the sexual and reproductive health game, because we may give this vaccine to a nine year old, but they become sexually active around age 16, 18, 19, as we see with our chlamydia rates, which are a really good example of what's going on there, despite what we say about protected sex.

So if we have a vaccine that's wearing off precisely when people are becoming sexually active, and we know from our experiences with chickenpox and other vaccines that wear off that, in fact, you can become sicker, what does that mean from an infectious virus perspective? I don't have the answer for that. I don't have the answer for that for the mothers and women who want to talk to me, and we need to know that.

● (1145)

[*Translation*]

Ms. Christiane Gagnon: Perhaps Mr. Carleton would like to respond as well? I know that it was under investigation in Europe. Will they prove there is a causal link? In a case like this, when Canada goes ahead with a massive vaccination—we are talking about Health Canada—should we not have a much more proactive attitude instead of waiting to see what will happen? For example, shouldn't they suspend the vaccination or impose a moratorium on it? Can you give us your opinion on that?

[*English*]

Dr. Bruce Carleton: Vaccines, just like drugs, have major adverse effects associated with their use, and death, of course, is the ultimate adverse event. What I would suggest is that if we want to have an effective post-market surveillance system, that means that when we actually provide the vaccine we collect data on the outcomes of interest and we collect it from both people who have reactions and people who don't have reactions.

In our case, I specifically went to pediatric hospitals and said "How many cases of cisplatin ototoxicity do you have?" They said they didn't know, they'd never looked at the hearing loss with cisplatin in a comprehensive way. So we began to uncover these cases. They're there, they're not hidden. And I would suggest that the same thing could be done with this HPV vaccine.

When women and girls are given this vaccine, their outcomes can be studied and the data can be collected systematically. We could have a sample of several thousand very soon. In my case, we collect biomaterial—saliva, or blood, or buccal swab—and we can look at whether the genes play a role in an adverse outcome in people who have the adverse effect versus those who don't. That's one way that we could deal with that issue.

Death occurs regardless of whether people get vaccinated or receive drugs. The question of causality is critical, and how to determine causality is extremely difficult. It's much easier to do when you can look at data from two sets of people who receive the vaccine—not just from people who had adverse reactions, but also people who didn't. That's what I would suggest would be a good approach in Canada.

The Chair: Thank you, Dr. Carleton.

Ms. Wasylycia-Leis.

Ms. Judy Wasylycia-Leis (Winnipeg North, NDP): Thank you.

Let me just carry on with this discussion.

It seems to me that what we're really dealing with is still the notion that women can be treated as guinea pigs. I'm wondering what has changed from the days of thalidomide, DES, the Dalkon Shield, and the Meme breast implant, to the point where we're at today with respect to, say, Gardasil and Evra, the oral contraceptive.

Is there any better protection for women, or are we still following strictly this risk-management model where we haven't studied the causality, we haven't made all the links, we don't know the cost-effectiveness, yet we put it out there and take the risk and we expect women to take the risk?

Madeline, and then Bruce.

Ms. Madeline Boscoe: I don't think it's changed that much, hence my suggestions this morning around both enshrining a requirement for sex and gender analysis but also trying to now move to some kind of richer framework for the evaluation of drugs prior to their approval, because I think we can make some prediction. If we say we know this drug is going to be used in 70- and 80-year-old ladies, that's who should be in the trial. If we think it's going to be used in nine-year-olds, that's who should be in the trial. It does change the way we do business, for sure, but I really agree with Bruce. We need to take the approach of a public health and population health management process.

I have to say as I think about this that the burdens on industry on managing all of this also seem somewhat unfair. We need to think of a system that runs from a public health process, that we're producing data and developing research and processes that actually are a seamless continuum, that look like a program, not a bunch of band-aids stuck together.

● (1150)

Ms. Judy Wasylycia-Leis: On that—and, Bruce, I'd like you to comment as well—it seems to me that things haven't changed to any great extent in terms of government being able to ward off big pressures from drug companies to push something on the market without the tests being done and without the precautionary principle being followed.

I'd like to go back to Gardasil, because the first that I know this issue came up in terms of the public and Parliament was when Merck Frosst appeared before the finance committee in Montreal, before the 2006 federal budget, pushing this vaccine. We hadn't heard about it before. We hadn't heard that this was an answer to a serious problem. And suddenly in the budget, without any further studies or talk, there appeared $300 million for a vaccine that may not have been fully tested or may not be fully cost-effective. So I'm wondering what we do to prevent this kind of situation from repeatedly happening, where drugs get on the market, treatments get on the market, and in effect often women are the guinea pigs, or maybe children.

Dr. Bruce Carleton: Okay, first of all, I think it's true that women are guinea pigs, but so are men and so are children in this environment, in that we're using drugs while having a limited understanding of their safety and effectiveness. Then we use them in the real world, so to speak, and develop a larger understanding of their collective value or concern.

Cost-effectiveness is a very difficult issue to deal with. I sit on CEDAC, the CADTH expert advisory committee that looks at cost-effectiveness. I can tell you personally that I find it an extremely difficult task, because we're looking at data from short-term clinical trials. In most cases we're talking about eight to twelve weeks of data by the time a drug enters the market. There can be more than one trial of that duration—sometimes longer, but often not. But uncontrolled experiments—in other words, the data on the use of drugs without a control group, just the post-market experience of users—are not very helpful in ultimately determining the drugs' cost-effectiveness.

So what we really need is much better data, longer-term data. I suggest that as a country of roughly 30 million people, we are not going to be able to change the international circumstances sufficiently and still receive, in many cases, the benefits of pharmaceutical products in ways that maybe the United States could muster with its buying power and its population.

What I would suggest is that we take an approach that recognizes our national health system, our collective ability to care for each other, which is phenomenally helpful in embedding networks and looking at post-market surveillance, and then when these drugs come on the market—and we presume their cost-effectiveness—we provide them under a framework that evaluates their true cost-effectiveness. It is better that we know ten years from now that a drug is cost-ineffective, and we stop paying for it, than to spend the next ten years wondering whether it is and talking about this ten years later, which is the current state of affairs.

I have spent more than fifteen years working with the provincial drug plan in British Columbia, a very frustrating fifteen years, in many cases, because there isn't a lot of interest in that kind of approach to drug coverage.

Ms. Judy Wasylycia-Leis: Let me ask another question to both Madeline and Bruce on this very issue, before my time is up.

Although the work of this committee is important, we also know that at the same time the government is pursuing its own post-market surveillance system and has put out a paper on strengthening and modernizing Canada's safety system, and has had some consultations and is preparing legislation.

So I would like to know from you, Madeline, first, whether or not you have participated in this and whether or not a gender analysis has been done of this whole approach. Second, what do you think of this whole shift toward a risk management model and a progressive licensing model which involves, according to the DM, implementing life-cycle approaches to regulating health products, thus shifting the focus from pre-market review to one that continually assesses a product's risks and benefits?

Madeline, and then Bruce.

● (1155)

Ms. Madeline Boscoe: I actually think this is a step forward in our thinking.

That being said, my remarks today were focused on two areas that I felt really needed enlightening. One was, of course, around sex and gender; but the other was about what that original bar was and what the risk management framework is. I think one can have a risk management framework and a company can say they are not going to do this because it is going to cost them $10 million.

As the Krever inquiry showed us, which is one of the reasons I think we are all here, to be honest—bless Mr. Krever—is that we did try at Health Canada to put a number on lives, and it didn't work out so well.

So I think a risk management framework saying that those dollars aren't on the plate, that the cost of that isn't on the plate, is okay. But that's where the commitment to a precautionary principle enshrined in the legislation will be an important piece, because it's the framework in which you can manage risk in a way that makes sense.

The Chair: Thank you, Ms. Boscoe.

Mrs. Davidson.

Mrs. Patricia Davidson (Sarnia—Lambton, CPC): Thank you, Madam Chair.

Thank you to both presenters. You've certainly given us a different perspective on post-market surveillance today, talking about the gender issue and the issue with children and so on.

I find the gender-based analysis to be very interesting. I'm involved with a study on gender-based analysis and gender budgeting on another committee I sit on, so this is something that I find very pertinent. One of the things that is happening is that gender-based analysis for policies, programs, and risk management is already a part of the mandate of Health Canada. I think you're aware of that and I think you made some reference to that.

How would you build further on this mandate to ensure that post-market surveillance of these products captures the significant differences that could be there for different genders as well as different ages? Further to that, how would we get around some of the ethical issues that we've already alluded to here this morning regarding testing for young children or testing for pregnant women—those types of things?

Maybe you both could speak to those questions.

Ms. Madeline Boscoe: In a way I'm here because twenty years ago women sitting around this table and in the House thought that sex and gender mattered, and we needed to develop infrastructure and knowledge to help. Someone very wise, a mentor in my career, said, “Madeline, you've got to know that it takes a generation”, and I guess it does.

Why I think we need to see things like sex and gender in drug reviews in law is because it's hard to do, tough to do, and costs to do it. I'm working right now with the Canadian Cochrane Collaboration, which as you may know the CIHR has funded to help improve the analysis of evidence. One of the things we're finding is because the Food and Drug Administration in the United States requires sex as an issue in clinical trials, there are an awful lot of women in these trials, but no one's analyzing the data. It doesn't make any sense to me. You think you've done it, and you think you can go home and do something else, and you take another look and you realize.

So I think we're a long way away yet. We're building the case. We have some few researchers. The Department of Health supports a program called the centres of excellence for women's health, which I think was originally a multi-party initiative, which is helping build the data that I'm able to show you. So we can show not that this is a morally right thing to do, but it costs us not to do it. On the issue of including it in a regulation, I think we need training. I still think we need third-party analysis and audit processes to help advance that. These are skills that people are still learning, from a drug reviewer to a policy analyst. I think that those of us in the community need to help step up to the plate to help train and build capacity in the department.

My own feeling is that when we took women out of clinical trials because they might get pregnant, that was a somewhat paternalistic approach to a very complicated problem. It's true that we gave thalidomide to women when we didn't know anything about its effects on fetuses, and we've definitely learned the hard way. But I think women are much more sophisticated now about that. We have drugs on the market that do harm fetuses if women are pregnant, and they are taking them. Touch wood—except for a few examples, it's worked out well.

So I hope that's enough.

● (1200)

Mrs. Patricia Davidson: I still don't understand how you get around the issue of the testing part of it. How do you get away from the thalidomides and those types of occurrences, if you're actually doing the testing on a pregnant woman?

Ms. Madeline Boscoe: You need to first start in animal models, and animal models are very helpful on the toxic effects of drugs on fetuses. That's one of the ways. The other way is for women who are now in clinical trials, one of the agreements, for example, is that they don't become pregnant, and if they do become pregnant, they need to understand the risks. So those processes are in place.

Particularly, let's go back to the Gardasil example and testing with young children. I think this is a much more complicated area because of the intimate ways in which evidence is done. Fortunately, there are some new tests that are on the market now, for example, for HPV that are just starting out that we could use with this age group without exposing them to intimate examinations.

Dr. Bruce Carleton: I think the issue of how to ethically involve children and women in clinical trials when we know or might suspect that there is a problem depends on the question you're asking. It depends on what you want to study. If what you're trying to study is an effective anti-infective for a serious infection that occurs during pregnancy, then the ethical boundary you're crossing to treat women in a clinical trial to determine its effectiveness while exposing them to a potentially risky therapy can be weighed against the potential benefits of that therapy. I think how we get around the ethical issues depends on the question, really.

Anthracyclines destroy the heart. There's a 61% mortality rate. They also cure cancer. So they're effective drugs, and we can get around the ethical issue of using them if we demonstrate that the benefit is more than the risk of the presumed toxicity.

Then there is early clinical trial monitoring. Already mandated are data safety monitoring boards to ensure that interim results are reviewed. Any safety signals that occur early in a clinical trial halt the clinical trial until further evaluation can be done. So we minimize the exposure.

There will always be a risk to using any drug in human life. There will always be risk, much like driving a car entails the risk of accidents. We can make them safer, much safer. I think understanding gender differences is important. Age-related differences are important. But I really believe that the serious effects we're talking about are largely genetically mediated, and that's where the heart of much of the science will push all of us. We'll be followers in this in the coming years.

The Chair: Thank you, Dr. Carleton.

We'll go to Mr. Temelkovski.

Mr. Lui Temelkovski (Oak Ridges—Markham, Lib.): Thank you very much, Madam Chair and both presenters.

I find this fascinating, Dr. Carleton. You mention a different sort of monitoring, which is genetic. You just finished by saying that we may be followers. Who would we be following? Are there other jurisdictions around the world that are much more advanced?

● (1205)

Dr. Bruce Carleton: I meant that you'll be following science. The science is there, and it's already been done. Warfarin genetic testing is being done now. Carbamazepine, a very well-used and well-accepted anti-seizure medication also used in some mental disorders, has a genetic test available to predict a rare reaction called Stevens-Johnson syndrome, which causes your skin to fall off. There are about 80 or 90 drugs that can cause that particular reaction. There is a genetic test now for people of Han Chinese descent, which is very important in Vancouver, to predict that kind of testing. This is already being done, and increasingly we'll see more and more of that.

It's not really a jurisdictional issue. It's really the science.

Mr. Lui Temelkovski: You also mentioned earlier that mandatory reporting doesn't work. I think that's why we're studying it, to make it, maybe, hopefully, more effective or to make it work.

Would more reporting of adverse reactions and, as you mentioned earlier, of no adverse reactions help?

Dr. Bruce Carleton: The system is 95% incomplete, so there has to be a massive increase in reporting, and the quality reports have to be there.

I favour a model in which we train clinicians, who are responsible for the recognition and reporting of adverse reactions, to do the work, and not just increase public awareness of reporting. It's great to have consumer reporting; there's nothing wrong with that, and I encourage it. But to get the substance of the reports we need, we really need dedicated professionals to monitor and evaluate drug responses. That's the information that will be most helpful.

In Spain it is a criminal misdemeanour to not report an adverse drug reaction, but it hasn't changed reporting. Vioxx was removed from the market because of Merck's own trial that confirmed the cardiovascular risk. No surveillance system in the world—mandatory or voluntary—picked up that risk, despite the fact it was the most frequently prescribed drug in the history of the world.

I suggest that surveillance systems run by governments traditionally haven't accomplished the goal of helping us identify significant risk in many cases. They can help in many ways, but I think we have to look to science to help us understand better ways to informed solutions. If we can have safety solutions we'll get reporting, because clinicians want safety solutions.

When I started my work I went to the oncologists at the Children's Hospital in Vancouver and told them what I was proposing to do. The head of the medical oncology unit said, “You know, it's an interesting study looking at the genetic basis of adverse drug reactions. We don't have adverse drug reactions in oncology.” That's either a sign of ignorance or arrogance, but it's neither; it's nomenclature. She doesn't think about reactions that are expected, like hearing loss and heart toxicity, as being adverse. She thinks of them as being a consequence of using the drug.

Now that they see that we can actually predict in whom the most serious toxicities are likely to occur, that's where reporting, funding, and support comes from. That's the way to get reporting. Maybe it's to mandate it, but it's to get individuals who are responsible for capturing these reports and individual institutions.

Mr. Lui Temelkovski: You mentioned that you've reported some of your studies and they're not yet published. Is there a filtering system there, from reporting it to publishing it?

Dr. Bruce Carleton: Right. We take all of the data we've collected and begin to go after specific reactions that we think are genetically mediated. We found three in the first six months, and we stopped looking at our data. We are still collecting and accumulating data, but we have a limited budget and limited resources. So we've concentrated on bringing these first three into a solution approach.

Instead of continuing to show a link between the drugs and genes, we're trying to bring these into a viable safety solution strategy for clinicians and patients who use those particular medications. So we started with serious morbidity, mortality reactions, drugs that are used in millions of patients a year, and risks that are at least threefold or more higher because of this gene trait.

The Chair: Thank you, Dr. Carleton.

Mr. Brown.

Mr. Patrick Brown (Barrie, CPC): Thank you.

Do you have any information on how other jurisdictions in the world deal with this in terms of females and children? Is there any evidence that systems are being adopted abroad that Canada could learn from?

● (1210)

Dr. Bruce Carleton: Sure. I'll start this time.

On the issue of other jurisdictions, in the United States the National Institutes of Health has a program called the pediatric pharmacology research units, or PPRUs. These were a result of modernization of the food and drug regulations, the FDAMA, the Food and Drug Administration Modernization Act, and a pediatric rule that was created particularly to allow for more testing. They created, really, an incentive for pharmaceutical manufacturers to do more pediatric testing early on in the drug development, and that has created a bunch of research units across the country to help produce better information about the kinetics of drugs.

Unfortunately, it's very much limited to the pharmacokinetics of drugs, pharmacokinetics being the way the drugs are absorbed, distributed, metabolized, and excreted from the body. It doesn't link in genetics at this point, although there's interest in doing that.

I think where Canada can add value to other jurisdictions is in areas like pharmacogenomics, in which we clearly are leading. I know we're leading because FDA came to see us in October. Along with seven of the major pharma companies, they formed a non-profit in the United States called the serious adverse events consortium.

Drug safety is one of those issues that pharmaceutical manufacturers definitely want to take on, now that Vioxx has been removed from the market. The reason they want to take it on is that they recognize it's a risk to their products and to their financial viability if drugs are pulled by them or by governments and safety concerns are identified. If they see a solution-directed approach, they seem to be interested. That's what they've created with the FDA: this way of taking all of these patients they have heard about or they may have collected information on and collectively look at whether there's a genetic reason or other common reasons that might be responsible.

They came to look because we have this embedded national network and they're interested in how we've done that. They can't do that in the United States. In the United States the hospitals compete with each other, even within the city. The international review team, when we began our work, told us that we'd never get this network set up even in Canada, and if we did we wouldn't find any biomarkers of drug risk. Well, we stopped looking after six months because we found three.

We did get the network set up. It took 18 months, but we did it. We feel with all the privacy issues, all the ethical concerns across the country, that every ethics review committee at every hospital and university in every province has to approve this, and that's all been done.

I think we have a unique value here by embedding such networks in the health care system that we can add to other jurisdictions, which other jurisdictions just simply can't do.

Mr. Patrick Brown: One thing we've heard before at this committee has been testimony on the progressive licensing framework. How would you suggest that gender- and age-based specific tests be incorporated into that?

Dr. Bruce Carleton: I'll start, and then I'll let you comment, Madeline.

Very quickly, I've spent a lot of time working with Health Canada, many years, and also the provincial governments. I have been profoundly shocked, perhaps, on the lack of progress in many issues. We seem to have the same meetings with the same discussions time and time and time again.

There was a meeting in March, a stakeholder consultation, a Health Canada round on progressive licensing. I missed that. I told them I would come to talk to them about what I've done. I met David Lee, the lead senior counsel there, and Maurica Maher, who's head of the progressive licensing framework. I actually think those guys have the right attitude to this, but what they need to do is focus on solutions. It's great to have a framework, a legislative framework, but it has to be solution-directed.

If you want safer drugs for women, pick a drug, pick a group of women to test the safety and the new surveillance system on. It's the same with children, the same with men—let's not forget men. These safety issues are for all patients and are important. There are gender and age issues that are important, but it's important that we look to decide which safety solutions we would like to come up with first. So have solutions in place that you're aiming for, not just a framework for licensing. It's great, but it looks a little bit like a Cadillac from, frankly, a car dealer who hasn't ever really built anything like that before.

They need to recognize that we need to have very specific objectives to improve the safety. Maybe it's about a vaccine like the HPV vaccine, to understand the determinants of the deaths that have occurred or other risks that exist. There are many, many drugs and many reactions to choose from. We just need to pick two or three and get our feet wet.

● (1215)

The Chair: Thank you, Dr. Carleton.

Monsieur Malo.

[*Translation*]

Mr. Luc Malo (Verchères—Les Patriotes, BQ): Thank you, Madam Chair.

Thank you to our witnesses for coming today.

Dr. Carleton, in light of the evidence we have heard, I had the impression that considerable information was available on the adverse effects of drugs. What I hear you saying is that in the end, very little is received. You said that only 5% of results were published or made available. Why?

My second question is a bit of a follow-up on the previous one. You also told us that the 5% of available data often contained incomplete information. Was it incomplete due to the type of study you were doing on the human genome or was it incomplete because of the comparisons that could be made?

[*English*]

Dr. Bruce Carleton: Sure. Good questions.

There are two points. One is the incomplete nature of reporting, and the other is the quality of the reports, which is what we're talking about.

So the first is incomplete reporting. Why don't people report? There are lots of reasons that people have cited. I believe, after having studied this for 20 years, that the reason people don't report is that there's no reason to report. What happens if I report an adverse reaction? Health Canada already knows about that one. This is well accepted. Those are some of the things that I hear from clinicians. They're not reporting reactions because they recognize that somebody already knows about them. They don't understand the purpose of surveillance. The purpose of surveillance isn't to uncover whether a drug is responsible. It really should be to uncover whether there's a solution to the drug safety problem that can be produced as a result.

In 2004, a group of researchers in Toronto in Canada found that for toxic epidermal necrolysis, the most serious form of skin reactions that occur from drugs like Bactrim or cotrimoxazole, actually where the skin turns black and falls off in very large sheets—it's largely fatal in most cases, an awful condition—most of the patients end up in Canadian burn centres. There is almost no non-drug reason for that particular reaction to occur. So they went to Canadian burn centres and said, "How many of these cases have you treated in the last five years?" I think that was the length of time. They found only 4% of those cases were actually reported to Health Canada.

So I think part of the problem is that people don't see a reason to report in terms of helping them find a solution to these problems. It's just another report of a reaction that's idiosyncratic, from the Greek *idios* meaning "compound" or "mixture" of reasons. We don't know why. So I want to find a reason why.

The second question you asked was about the quality of reports. Why are the reports that come in not complete? And it's not just my reports. It's the ones in Health Canada, the ones I've seen through the Canadian pediatric surveillance program, the ones I've seen for the network I've built in the United States. The reason they're not complete is the physicians tell you the information they think you want to know. So if they think the purpose of reporting is to link drug and reaction, they'll report "Paxil: suicidal thinking", and then sign their name. They don't provide all of the other information that's useful to determine the biological reason for the response, because they don't understand how you're going to use that information or how it's being used.

So I think that's part of the problem. We have to do more than just sell clinicians on reporting for the public good. We have to show them why it's useful—because we can get solutions.

I found when I built the network across the country that oncologists didn't want to participate in it initially. But once you start showing high odds ratios, high risks associated with a particular gene trait, they start to listen. The arms become uncrossed and they begin to listen and move to the edge of their chair and provide funding. Once they see a solution possibility, they begin to report. So I think those are the reasons why.

The Chair: Did you want to make a comment on that, Ms. Boscoe? You sort of raised your hand, so I wondered.

Ms. Madeline Boscoe: Is that okay?

The Chair: Please go ahead, absolutely.

● (1220)

Ms. Madeline Boscoe: I want to link it to the other question too. There are elements that we can learn around surveillance that I think Bruce has alluded to that have been a standard in public health. We do select doctors and nurses and pharmacists to report. We train them up. Sometimes it's on how much measles is going on or how much pneumonia they're seeing. What we haven't done is train up our professionals to do this in such a robust way. It's partially because people don't see a circle. They see a black hole.

The other piece that I think you've had before you is the proposal for the drug research and effectiveness network, which would be tasked with the job of developing how to synthesize this information, how to do the follow-up studies of the kind that Bruce is involved with and developing a hierarchy of needs. But I just can't stress enough that we need a framework going into it that will make sure that we're covering off the bases so that we are including sex and gender and we are including data on age at the beginning, otherwise we won't have it at the end and we'll be back here again just repeating the wheel.

I think those processes are in the planning stages, and I would urge you to bring Dr. Lee back.

The Chair: Thank you, Ms. Boscoe.

Mr. Tilson.

Mr. David Tilson: Thank you, Madam Chair.

I'd like to ask a question with respect to money and availability of personnel. This question has been asked to other people.

Right now, as I understand it, in Canada, the only mandatory reporting for serious adverse reactions is from the pharmaceutical companies. Of course, there are others who could do it. Doctors could do it. Pharmacists could do it. I suppose nurses could do it; I don't know. But then you get to the question—and I'd ask both of you to comment, you as a nurse and you as a doctor—that they're all saying we don't have enough doctors and we don't have enough nurses. I guess we have lots of pharmacists—that's probably not a nice thing to say, so I withdraw it. But that's a comment that's made, that we don't have the professional personnel you're talking about with respect to tests.

Dr. Carleton, you mentioned tests after vaccines, that the doctors should make some reporting right there and then, and one of you made a comment about professional trainers, to do this reporting. So the response we're getting back—and it's common knowledge, because all you have to do is look in the papers every day—is that we don't have anybody to do these things.

Ms. Madeline Boscoe: You're right. I think we need to be cognizant of the fact that we need to be managing our human resources in health care. We have some gaps, and we do need to develop a plan. I totally agree.

People my age are all hoping to retire, I think, but the act of reporting, itself, is not that difficult. We are, more and more, working in an electronic record process. Physicians frequently now bill the health system through an electronic process. So we're not talking about something particularly robust.

The professional training of physicians, nurses, and pharmacists, updating them on whatever it is, goes on all the time. This would just be in the queue of how to do effective surveillance, just as we are out there teaching them how to do an electronic medical record or whatever other new skill set they need. I think it needs to be implemented into that queue, but I don't see it as a huge challenge to operationalize, because they're in the business of reporting already. There are nurses in this country who count how many kids they saw with colds and flus. There are physicians who phone in odd things.

Mr. David Tilson: The Canadian Medical Association may disagree with you.

Dr. Carleton.

Ms. Madeline Boscoe: Well, I'm sure they would.

Dr. Bruce Carleton: We can train physicians and nurses and pharmacists to do their reporting. In the United States, where MedWatch came in with great fervour that it would increase reporting in 1996, in 1997 there was a 50% increase in adverse drug reaction reporting as a result of the online registry that FDA set up for consumers and health professionals to contribute reports to. That improvement, hundreds of millions of dollars in the creation, results in one report every 336 years per physician and one report every 26 years for pharmacists. So pharmacists are actually much more effective at reporting than physicians.

But it's getting the quality of reports in a thorough and standardized way. It takes me four hours to put together a cisplatin deafness case. This is not an inconsequential amount of time and energy for a health professional to put together. We need professional surveillors. At the moment, your hospitals across this country all have a clinical pharmacist. Clinical pharmacists all have the mandate to report adverse reactions. It's part of their job descriptions, I would bet, for all of them. If it isn't, it should be there. Unfortunately, it's just one more task added on to the long list of things they already have to do.

The best way to do this is to get a handful of people together and make it grow from there. I have 13 people across the country, and in three years I have more than 9,000 cases and controls, more than 1,000 serious ADRs and more than 8,000 controls, which is what I need in order to look at the heterogeneity and response—13 people.

● (1225)

Mr. David Tilson: I have a question, Dr. Carleton. A drug is approved—

The Chair: Mr. Tilson, I'm sorry, your time is just about up, so I'm just going to let you know that. You have about four seconds.

Mr. David Tilson: Four seconds.

The Chair: There you go.

Mr. David Tilson: I can't do it.

The Chair: Okay, thank you. I thought you could do anything, Mr. Tilson.

Ms. Wasylycia-Leis.

Ms. Judy Wasylycia-Leis: Thank you.

I want to come back to adverse reactions and reporting. We've heard a lot of testimony about the fact that mandatory reporting might not be the most effective way to go or the best use of anyone's time. Yet we have situations—and some of the things we've already talked about today—with drug companies that collected information around the world and yet chose not to report it. I think some of the information that came out around Vanessa Young's death has been helpful in that regard. I think some of the stories around EVRA, the oral contraceptive, where women are dying because of blood clots, suggest that there needs to be some way to hold drug companies accountable for information they garner.

What's the best way for us to get that? Is it full disclosure? If it's not mandatory reporting, then what is the next best way we can make sure that information is shared and consumers at least have the information they need to make sound judgments?

Ms. Madeline Boscoe: I guess I'm a believer in mandatory reporting as a component. Partially why I put my energy into supporting the drug research and effectiveness network is it would be the backbone that would support researchers like Bruce, doing what I would call communities of practice; that is, we would use the surveillance methodologies that are already in place to drill into practice communities—whether it's birth control providers, if we think about EVRA and the patch, cancer communities, if we're thinking about cancer—so that the providers that are working with those drugs understand their engagement and involvement in this post-marketing effort. It doesn't mean that we don't have a general information database.

But the other side—and this is what I call phase two if I had a work plan in front of me—is to build communities of practice, and I'm using those words, because I think it is about reflection, discussion, and having a closed feedback loop. It's what we knowledge-brokers call communities of practice, because that gets to the specificity and the richness of the data, but it allows us a sentinel function. When you put a canary down a coal mine, it doesn't tell you what killed it. It just tells you it's dead. Well, in a similar way, we need a canary methodology—that's what adverse drug reporting in a broad way is—but we need to support these communities of practice that will actually do the day-to-day detailed development and the rich analysis that's needed.

I infer that Dr. Carleton's work is also around saying we need some of the biologics to help us inform that. That should be part of the road map plan too, with the sex and gender analysis.

● (1230)

Dr. Bruce Carleton: My comment is that mandatory surveillance is great in concept but very poor in execution. It's very difficult. How are you going to regulate it? How will you know if somebody didn't report? How are you going to enforce it?

The difficulty for physicians, nurses, and pharmacists is that we have things like suicidal ideation occurring with antidepressant use, but those are background events that occur as a consequence of the underlying depression as well, so how do you separate out what really is an adverse effect of the drug—a negative health outcome—from an underlying disease? Those issues become very difficult to sort out. We spend an awful lot of time trying to regulate and manage clinicians to report things whose basis we don't really understand.

I prefer a solution-directed approach, which says that this is a particular reaction we're worried about. In the case of EVRA, I think we're probably going to find out it has to do with the delivery system—that we may have an increase in the release of hormones that's inordinately high from this particular patch. I don't know the answer to that, but a solution-directed approach would try to uncover the specific problems related to EVRA. I think we would do better if we concentrated on finding specific health issues and specific drug issues that we were concerned about and worked towards specific solutions. They're going to be different, depending upon the issue.

I don't favour mandatory surveillance, because I don't think it's going to work. It would be great if it did; I just don't think it's going to work. You need quality reports as well as numbers. Getting numbers isn't sufficient. You have to have quality in the reports; otherwise, it's useless.

Look at how many reports manufacturers provide already. They're mandated. There are hundreds of thousands in the United States; they're virtually useless because the lack of clinical information that's included about the patient is a predominant problem.

The Chair: Thank you, Dr. Carleton.

Go ahead, Mr. Fletcher.

Mr. Steven Fletcher: Thank you, Madam Chair.

If you're looking for a canary, I can always volunteer my colleague here, David.

I'm going to show my Manitoba bias by asking Ms. Boscoe several questions. I'll ask them all at once, and then my time will be up, I'm sure.

The HPV issue is something the government takes very seriously. We invested $300 million in the vaccine. I am intrigued by one of the statements you made right off the bat, and that was—I hope I wrote it down correctly—"They die of lack of care, not of the disease". I wonder if you could expand on what that actually means. Perhaps the vaccine isn't the whole solution. If you were to take the vaccine and also follow up with diligent care, that would reduce the mortality rate significantly, I would hope. I'd like to hear your point of view on that.

Also, in your opening statement you mentioned that you co-chaired a committee on Infoway. I think everyone agrees that there's an importance in post-market surveillance; it's the mechanisms on how to do that....

Do you have any insight or recommendations for this committee that we could put in our report that deal with Infoway or e-pharmacy or e-health records, insight or recommendations that would allow data mining or make it easier for medical practitioners to report? Four hours on one issue is a long time. You could see a lot of patients in that time, and you're probably not getting compensated for the time you're spending on reporting. Are there ways through Infoway and e-technology to make this an easier process? You seem to be in a good position to comment on that, given your background.

Those are my questions.

Ms. Madeline Boscoe: Okay.

Vis-à-vis the HPV issue, as I said before, this could be the best thing since sliced bread. Our position at the clinic has been that it's premature to have put it into the population base until we knew how long it lasted and whether or not the viruses that are in it actually are the ones that women and men are being exposed to. We have some sense in Manitoba that they may not be.

Those are big issues, because if it wears off, what are we going to do? If we take the model of chicken pox and others, you actually get sicker when the vaccine wears off. And as you may know, repeat vaccination after school in adults is totally related to socio-economic issues; that is, people who are poor and the children of people who are poor are much less likely to revaccinate or to become vaccinated. It's a health equity issue, and the reason that's important in sexual and reproductive health is that the other burdens of problems with sexual and reproductive health also are borne by people of lower socio-economic areas.

What we know about access to cervical cancer.... And we have made such a huge impact. The rates of death in Canada have plummeted. In Manitoba, we have about eight to eleven deaths a year right now. Of those women, the vast majority were in care but didn't have a Pap test in that timeframe. How can that be?

I would plead that some of that investment needs to go to places that are women-friendly, that provide female physicians, that do outreach to women to get them into care. That's what I meant by "They died of a lack of care". They saw a doctor; they just didn't get what was needed. Women with disabilities, poor women, and women with addictions are particularly challenged in this area.

Regarding the info highway, I have two pieces I can speak to on that—which gets me to the part I didn't even get to talk about. How convenient is that?

It is true, the electronic medical record will help us with this. These investments that are being made to help develop these systems will help.

The other piece is an electronic reporting process itself—not a web-based one, but in the same way that physicians can use a Palm Pilot to send off a bill to every provincial government, they could fill this out as well.

I hope I answered that piece. But I also wanted to talk a little about increasing Canadians' capacity in drug policy.

Canadians believe right now that if it's approved for use, it's a great drug and should be on a provincial formulary—I'm sure, if you talk to your provincial counterparts. They can't believe and they don't believe, if it's approved for use, that it is much of a risk for them, because they believe that has happened.

So we have a huge problem in what our patients understand an "approved" drug to be and what it means. This means increasing their ability to be thoughtful consumers and understand what's going on in their own bodies.

● (1235)

The Chair: Time is running out. Can you...?

Ms. Madeline Boscoe: Yes.

The other big ticket I think we can do is to take the intellectual property rights for the patient insert and the drug label and make it a public good. Health Canada can put this information up on the website, change it when it needs to, and send out alerts tied to that information.

The Chair: Thank you, Ms. Boscoe.

Monsieur Thibault.

Hon. Robert Thibault (West Nova, Lib.): Thank you very much.

I want to thank you both for your presentation.

Last week I was convinced that we wouldn't hear anything new, and we did a bit, Dr. Carleton. I think you're taking a new take on something we've heard.

One of the things we've heard from many practitioners is that making it mandatory without making it useful has no value, and if you make it useful you don't have to make it mandatory: people will voluntarily participate if they derive benefit from it. Practitioners, if they have some activity happening and can go to one page or site and say "This is the adverse event I'm experiencing with this patient" and get back useful information, would participate.

But what you're advocating is a little different, I think. What you're advocating is a specialization across the country of people who are doing in-depth research on individual cases to build the database.

Have you talked about bringing it that one step further and marrying the two, such that you would have online reporting of incidents by practitioners and then the information that you have discovered could be the feedback? It would serve as a database for you on where you send your specialist to do these studies of cases. You might start seeing a lot of commonality, a lot of bunching. Those would be the first cases you would want to investigate fully.

● (1240)

Dr. Bruce Carleton: It's a worthwhile goal; it's a worthwhile thing to pursue. The difficulty is resourcing this, because physicians, pharmacists, and nurses report the information they think you need to know. The four hours to put together one cysplatin case comes from experience and looking at many, many of these cases, and understanding what information I need, and specifically how to deal with differences in the information that's collected. Audiograms, the way you measure hearing, are done with different equipment, different standards, different thresholds across the country in different hospitals. Those kinds of differences have to be accounted for. If physicians just report reactions or Palm Pilot reports, it's not that useful. We need the in-depth information surrounding the case. If there's a way to identify the case, the physicians can give us a case and help us identify them, fine, but I can actually do that within hospitals fairly effectively now.

I would like to involve as many people as possible in adverse drug reaction reporting, but I think it's better to start small and then move to a bigger palette across the country and involve more and more practitioners. I think if you show some key successes with a few people, small projects, you'll get more people who want to participate and then a groundswell of participation continues. I think that's way better than building a national system of reporting and then having to staff all the sorting out of the reports. The difficulty with sorting out the reports is that they don't give you all the information you really need.

Hon. Robert Thibault: The other information, the other difficulty, is what is "useful information"? What is going to be useful to the practitioner in his day-to-day practice, and what is going to be useful to the patient in the decisions they have to make as to what level of risk they're willing to take? I remember when you were opening your presentation you made a distinction between adverse effects and side effects, but one can be the other. If I have a child who is at great risk of dying of cancer, and they have a drug they can give him, but the chances are, I believe you said, 60% that he'll have some heart disease because of that drug, if it's going to give him a reasonable chance of living, I'm going to consider it a side effect. If I know in advance that I'm taking this decision, that there is a risk, it becomes a little bit of a line as to what information you have as a practitioner or as a patient in the decision that you make. If I have severe enough pain, I might want Vioxx, and I'll accept the risk of the cardiac event that could ensue.

Dr. Bruce Carleton: The holy grail of pharmacogenomics would be to determine alternative drugs or different doses of the same medication that should be used, based upon the patient's own genetic profile and how they process the drug. The difficulty in getting there, though, is still a problem.

Even predicting in whom the reaction will occur is of benefit, because in our very large provinces, getting people for routine testing, for cardiac testing, from the Queen Charlotte Islands, for example, is a bit of a problem for us, getting them all the way down to Vancouver. We sometimes can't get them to Vancouver for cardiac testing, so we have to wait until their next scheduled visit. If we knew predictably that they were at a higher risk of a reaction, we'd ensure we did more routine testing, and perhaps even have testing facilities and the right kinds of qualified professionals in a closer location to where they live so that could be done routinely.

The Chair: Thank you, Dr. Carleton.

I want to thank both our witnesses today, Ms. Boscoe and Dr. Carleton. This was a most interesting and informative presentation. It's very exciting to hear some of the new ideas that have come forward. I think the whole committee can substantiate my comments, because we were truly taken with both your presentations.

We have committee business now, and I'm going to ask that you leave the room rather quickly so we can get to that committee business, because at one o'clock sharp we have to get back into the House.

I want to thank you again so very, very much for your contribution today. Thank you.

[*Proceedings continue in camera*]

Published under the authority of the Speaker of the House of Commons

Publié en conformité de l'autorité du Président de la Chambre des communes

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