Protecting Our Health:
# New Debates

**Women and Health Protection**
in collaboration with *DES Action Canada*

# Who Benefits:

## International Harmonisation of the Regulation of New Pharmaceutical Drugs

The public has the right to expect that all new pharmaceutical drugs are fully tested and that the highest possible safety standards are met. Citizens rely on government regulators to set standards for drug approval that are in the public interest. This brochure explains how the push to streamline the drug approval process in the world's three largest pharmaceutical markets is neglecting the special needs of women. It also addresses how this process may be compromising overall drug safety standards and jeopardising access to affordable medicines.

For the last 12 years, a pharmaceutical industry/government organisation called the International Conference on Harmonisation of Technical Requirements (ICH) has been working to blend the approval process for new pharmaceutical drugs from Europe, the United States and Japan into one set of standards.

While not a voting member, Health Canada has participated in the ICH and declared itself "committed to the principle of harmonisation." To date, Health Canada has adopted the vast majority of ICH guidelines through regulatory change.[1] There was no public debate, in Parliament or more widely, about Canada's adoption of ICH guidelines.

Yet ICH guidelines will have a direct impact on the safety standards used by Health Canada when it approves new medicines and, perhaps, an impact on the availability of less expensive drugs.

## Women and ICH

This brochure describes the ICH process, focusing on the changes to drug regulation that are likely to have a negative impact on safety. It will especially examine how changes in drug testing standards can affect women. ICH proposals completely ignore the need for special research guidelines for women. Women use more medicines than men and are vulnerable in different ways. They have been disproportionately affected by some of the major drug disasters in the past that could have been prevented through better regulations, such as DES (diethylstilbestrol) which is described at the end of this brochure. And women are still disproportionately affected: of the ten prescription drugs withdrawn for safety reasons from the US market between 1997 and 2001, eight affected more women than men – half of those drugs because more women took them, half because women were more vulnerable to the drugs' harmful effects.[2]

### ICH membership

The home base for the ICH is in Switzerland at the International Federation of Pharmaceutical Manufacturers' Associations (IFPMA). The key participants in the ICH – the only ones with votes – are the three brand-name pharmaceutical associations that represent that industry in the United States (US), the European Union (EU) and Japan, and the three government health agencies for these same areas. The US, EU and Japan are the three largest pharmaceutical markets in the world -- together they represent close to 80% of the world market – and they are also home to the world's major multinational pharmaceutical companies. (For detailed information on ICH on the web, you can visit http://www.ifpma.org/ich1.html)

Soon after the International Conference on Harmonisation was officially formed, in 1990, representatives from the World Health Organisation (WHO), the European Free Trade Area and Health Canada joined as non-voting observers. There is no direct representation from companies or government agencies from developing nations, public health advocacy groups, the broader medical profession, or the generic drug industry, which manufactures prescription drugs after brand name patents have expired.

# Why an International Conference on Harmonisation (ICH)?

**Trade battles.** Trade initiatives played a key role in the formation of the ICH. In the mid and late 1980s, the US and Japan began trade talks that included discussion of opening up the Japanese market for US pharmaceuticals. In response, the European Commission strengthened its resolve to establish a single EU standard for drug approvals in order to be competitive with Japan and the US in international trade negotiations. The International Federation of Pharmaceutical Manufacturers' Associations responded to these competing trade initiatives by organising meetings between the EU, Japan and the US.

**Faster approval.** The driving force behind ICH is the pharmaceutical industry. Prior to ICH, a multinational company was required to conduct a variety of studies and follow different government regulations in order to get its new product approved for patient use in different countries. The industry was interested in streamlining this process in order to reduce development costs and reduce the time to get drugs to market. These changes would allow trade name pharmaceutical companies to reap greater profits from a drug because a shorter part of the patent protection period is spent in the pre-marketing phase. The patent clock begins ticking from the time that companies file an application for patent, so the quicker the drug can get to market, the longer the exclusive sales period.

**ICH is advantageous for the brand-name pharmaceutical companies.** To bring drugs to market as quickly and inexpensively as possible, and in as many countries as possible, the pharmaceutical industry needs the ICH to:

- agree on one set of scientific rules for running clinical trials;
- reduce the number of research animals and human test subjects necessary for testing (thus reducing expenses);
- establish one set of standards for the manufacturing process of new drugs;
- ensure similar application processes for drug approval in all countries;
- ensure that research findings from one member country will be accepted by all other countries (with some exceptions for special populations).

All of those measures would help to bring drugs to market more quickly. No one would disagree with doing away with unnecessary and uninformative duplication of

research. However, when it comes to cutting corners and shortening timelines, it's another matter. For most of the public, speed of approval is not the major consideration. More important is protection of public health, and new medicines that have been thoroughly tested for safety and that meet real human needs. If the ICH process leads to compromises in safety standards through a rush to "harmonise" to the lowest of existing standards, there is good reason to be concerned.

## Concerns about ICH Guidelines

This brochure cannot discuss all ICH recommendations in detail, so the main focus will be on those that raise the greatest concerns for public safety and for women's health.

The key focus of ICH is on getting drugs to market more quickly. From a public health perspective, this drive does not benefit the consumer unless the drugs brought to market more quickly are new drugs that meet significant unmet health needs, such as providing treatment for previously untreated or inadequately treated life-threatening illnesses. Otherwise, there are strong safety disadvantages to rushing to market with drugs that duplicate those already on the market ("me-too" drugs) or novel drugs that represent only minor advances (such as new flu drugs with marginal effectiveness against symptoms). Rushing such drugs to market can lead to confusion and over-

### Canada's Role in the ICH:

- Canada accounts for only two per cent of the global pharmaceutical market and was not a major player in the various competitive trade initiatives that led to the ICH.
- Still, Canada joined the ICH shortly after it was formed and is the only single country given observer (non-voting) status. This grants Canadians influence, but not voting power. (The European Free Trade Area, which also has non-voting status, represents a group of non-EU countries in Europe).
- The department within Health Canada that regulates pharmaceutical products is called the Therapeutic Products Directorate (TPD). The TPD acts as Health Canada's representative to the ICH .
- Since 1993, the TPD has adopted all but a half dozen of the ICH guidelines.[3]
- There has been no parliamentary debate or government legislation with respect to Canada's involvement with the ICH and its adoption of ICH guidelines.

prescribing, as companies compete fiercely for a limited market or push to create a demand. Rushing such drugs to market can compromise safety (because the safety profile of new drugs is incomplete), lead to increased costs (since new drugs are almost always more expensive than older drugs) and undermine the use of older drugs with established safety profiles.

**Speed of approval is not our only area of concern:**

1. Public accountability is missing in the ICH process.
2. ICH has not addressed the problems women currently face with drug regulation.
3. Some ICH changes are reducing the safety tests during clinical trials, and thus potentially weakening public health protection.
4. ICH is not concerned enough with drug safety once the product reaches the market. Stricter, mandated regulation is needed for post marketing safety.
5. Changes in manufacturing quality standards as a result of ICH may limit competition, raise the costs of medicine and threaten the production of inexpensive generic drugs.
6. The ICH will streamline the process to get a new drug approved, but will these new medicines meet real health needs?

## Measuring Drug Efficacy in Different Populations – including women!

A key requirement of any new medication is that it must be effective and safe in treating the condition for which it was designed and for all of the populations that will be using it. Even before ICH, drug testing had fallen short in ensuring fair representation of all populations. Pharmaceutical companies rarely include enough women, elderly people or ethnic minorities in trials so that effectiveness and safety can be assessed separately for each of these groups. With the advent of ICH, companies can now get approval with even fewer test subjects.

To address this concern relating to fair representation of multiple populations, the ICH created detailed guidelines for companies on ensuring ethnic representation, geriatric representation and pediatric standards.[4] There is, however, a complete absence of ICH guidelines on women in clinical trials. And this is despite the fact that both the US and Canada have for many years had well-respected policies and guidelines on inclusion of women in clinical trials.[5]

- It is imperative that the ICH create a Working Group on Women, using US and Canadian guidelines as a starting point.

- ICH member companies should be mandated to enrol women in all clinical trials of drugs that will be used by women, in numbers sufficient to be able to separately assess drug effectiveness, safety, side effects and dosage levels for women as compared to men. Government regulators, such as Health Canada, should ensure that adequate monitoring and enforcement of these guidelines take place.
- One provision in the guidelines on geriatrics must be challenged and changed. It states that sponsors (i.e. drug companies) can determine that they are exempt from including the elderly when conducting a study. But only government regulators should be able to make such exemptions. The elderly are often more sensitive to the harmful effects of medications and more vulnerable because they

## A "Special" Population:

Women have historically been under-represented in drug research trials for fear that if they are, or become pregnant, the drug could cause birth defects in the child to be born. Enough women should be involved in all stages of drug development so that safety and efficacy can be analysed separately for them. Results from male-only studies cannot be generalised for many reasons, including the following:

- On average, women are smaller than men. Most serious side effects are thought to be dose related. When women take dosages designed only for men they are possibly getting a higher dose than may be safe. Although dose-ranging trials are now more common, there is no mechanism in place to ensure that such trials include separate analyses in women to see if the drug works differently, so that appropriate dosage can be determined.
- Some drugs have adverse effects that women are known to be biologically more prone to than men, including cardiac effects like QT interval prolongation.
- Several drugs are known to be metabolised at different rates for women than men or are eliminated from the body in different ways. This can also affect the dosage women should be prescribed.
- Some drugs, such as birth control pills and hormone drugs, decrease the effectiveness of other drugs. Some drugs, when used in combination with specific other drugs, have unwanted side effects. On average, women use different combinations of medications than men; hence drug interactions that might occur in women will not be picked up if they are not analysed separately.
- New research indicates that the menstrual cycle, menopausal status, or hormone replacement therapy can influence a woman's response to medications and dose levels. Therefore, adult women of all age groups should be included in research trials.
- It is now recognised that women of childbearing age need not be excluded from research - as has historically been the case - as long as they are using effective birth control methods. While such women are now more routinely included in clinical trials, in large part because of requirements introduced for US market approval, not enough are included in order to separately analyse the data. Women are also omitted from some of the earlier 'phase I' trials in healthy people.

may take several medicines at once. Drug approval should be denied to any sponsor that does not apply to regulators for an exemption in advance, and that fails to include the elderly in their clinical trials of a drug that will clearly be prescribed for significant numbers of older adults.

***A drug should be tested on the range of types of people who are likely to use it. If especially vulnerable people are among the potential users, trials in these groups are necessary.***

## Safety Guidelines during Clinical Trials

The ICH has challenged the necessity of particular safety checks on new drugs.

**Testing for Cancer Risks and Adverse Drug Events.**
Animal testing is carried out to make sure a new drug is safe for eventual human use. The ICH wants to minimise the number of such tests because of financial concerns (reducing pre-market testing requirements helps speed the process of getting drugs to market) and controversy over the use of animals. However, without a suitable replacement, reducing animal testing could expose Canadians to significant cancer risks or toxic side effects:

- Two long-term animal studies are usually used to ensure that a new drug is not carcinogenic and does not cause other serious harmful effects.

- Historically, cancer-risk testing is performed on two different rodent species (usually the rat and the mouse). Studies have shown that results from two animal species are better predictors than from one alone (although testing on rodents does not guarantee drug safety, as with thalidomide).

- Clinical trials on humans are only supposed to begin after an experimental drug passes all of the animal safety checks.

**Despite the above,**

- An ICH guideline recommends that, unless there is a special concern for the patient population, large-scale human clinical trials lasting up to one year can begin in the absence of completed carcinogenicity studies in rodents. In other words, trial participants could be exposed to an unknown cancer risk. It is unethical to expose trial participants to an unknown cancer risk when waiting six months to one year longer would add the results of animal trials.

- Although its own data on reducing standards was inconclusive, the ICH now recommends that only one long-term rodent cancer study needs to be conducted, plus one other short or medium-term study. This eliminates the safety of two long-term studies on two different rodents.

***Health Canada should not adopt any ICH guidelines that reduce long-term testing, or testing of two rodent species, unless there is reliable scientific evidence that another model is equally valid.***

**Testing for Repeat Dose Problems.**

In another phase of testing, animals (non-rodents) are exposed to large or repeat doses of an experimental medication to ensure that the drug does not become toxic above certain levels. Before the ICH, the US required 12 months of such testing, while in European countries only 6-month toxicity testing has been required prior to marketing approval. When it set out to harmonise these two systems, the ICH concluded that it was not advisable to reduce the repeat dose testing to 6 months because the US Food and Drug Administration proved that some cases of toxicity only showed up by 12 months. To protect the consumer, the ICH should have adopted a 12-month standard. Instead, an ICH Expert Working Group concluded that a study of 9 months duration should be long enough to detect toxicity. Equally problematic was that it didn't even impose nine months as a minimum standard, but rather as a maximum one.

An industry representative acknowledged that science was heavily influenced by political considerations in reaching this guideline:

> "It isn't pure science. There you are in the US where drugs have always been tested with a year's toxicity and suddenly because of some negotiating with Europe, you're now reducing the safety margin on drugs being tested [to 9 months]... I think the EU had to be very careful about the public reaction which says 'hey wait a minute, all these years we've had drugs on the market which were only tested for 6 months and now you're telling us they should have been tested for 9 months... "
>
> *interview by John Abraham with a representative of the IFPMA.*

***Patient safety must be rigorously protected. The ICH, and Health Canada, should ensure that a standard of 12 months toxicity testing be required.***

## Post-Marketing Safety Data

Once new drugs are approved for use, governments must still monitor their safety. Sometimes side effects don't show up in a research group of 3,000 volunteers, but become obvious when drugs are used in larger populations. Interactions with other medicines are not uncommon and can't always be assessed in a pre-marketing research trial because patients taking other medications are excluded from these trials. Similarly, a drug can have adverse effects in particular populations who were excluded from pre-marketing trials. This is why it is crucial to follow a new drug after it has been approved for use.

**There are some areas of concern about the ICH deliberations in this area.**

- Harmonise up or down? Most countries involved in the ICH require companies to file "Periodic Safety Update Reports" (PSURs) for new drugs. (Canada does not, although it is currently reviewing this.) The US currently requires PSURs every four months during the first 3 years after a drug goes to market. The EU and Japan require PSURs only every 6 months. Waiting for 6 months to find out that a newly-marketed drug is having more harmful effects than anticipated is too long. The ICH is still debating this standard, but should harmonise these requirements upwards to the US standard to protect public health. In this instance, Canada should follow the US model.

- Companies are required to report increases in the frequency of adverse drug reactions. However, no rules are in place to make sure companies monitor how often adverse drug reactions occur or at what point they must report an increased frequency; this is left to the discretion of the company. This is unacceptable since significant increases in the occurrence of known Adverse Drug Reactions (ADRs) have not been reported in a timely manner by companies. The ICH should provide a clear-cut, enforceable standard for changes in ADRs occurrence that would trigger reports. The ICH's guidelines on PSURs cover how and when companies report to regulatory agencies. But such requirements have limited impact unless government regulatory agencies require:

- mandatory, active follow-up of drugs once marketed,

- a rigorous system of reporting by health professionals if their patients experience an adverse reaction,[7]

- clear instructions to physicians about what to report,

- mechanisms for allowing consumers to make direct reports,

- assurances that the information will get out quickly to the public and health professionals in a manner that will maximise the response to these alerts.

## Brand Name Protectionism?

ICH guidelines have set new manufacturing standards for pharmaceuticals. The ICH argues these new standards will benefit the public, but others, such as the World Health Organisation, are concerned that these new 'gold standards' for manufacturing may provide little true therapeutic benefit and may additionally have other effects:

- Changing manufacturing standards may raise costs. Large multinational companies can afford to implement climate controls and other new lab standards. Smaller brand-name companies, however, may be hard pressed to meet ICH protocols and stay in business. The result could be reduced competition and higher prices.

- Developing nations may be hardest hit as local production of medicines might become impossible if these countries adopt the ICH standards or if domestic companies in these countries find that they can no longer export their products because they do not meet the ICH standards. In the latter case, production purely for the domestic market may not be economically viable and companies may be forced out of business. Already, developing nations are forced daily to make difficult choices between purchasing new medications from developed nations at prohibitive costs, prescribing only older medications (which may have a better safety profile), or breaking patents to purchase cheaper equivalents or, doing without useful drugs.

***Health Canada should press ICH for evidence of public health benefits from the quality standards, rather than blindly adopting the latter.***

**Generic Drugs and the ICH:**

After a trade-name company's 20 years of patent protection has expired, a generic company can manufacture an equivalent drug and sell it, usually at a significantly lower price. Health Canada is recommending that the new ICH drug manufacturing standards be applied to the production of generic drugs. This is despite the fact that the ICH was not designed to discuss generics – indeed, the subject was supposed to be the regulation of new drugs -- and the generic industry is not formally represented on the organisation. After a trade-name company's 20 years of patent protection has

expired, a generic company can manufacture an equivalent drug and sell it, usually at a significantly lower price. Recently, at the insistence of US regulators, the international generic industry has been invited to have observer status on a limited number of issues selected by the ICH. A generic industry spokesperson says that while some aspects of the manufacturing standards make sense for the generic industry, others simply don't.

***Health Canada should only implement new manufacturing standards for generic drugs in agreement with the Canadian Generic Pharmaceutical Association.***

# New Medicines – Do They Meet Real Needs?

## The Promise of Innovation

Industry and government participants have justified the ICH process on the basis that money saved as a result of harmonised regulations could be used for innovative research, creating necessary new drugs. But fewer than 9% of new medicines approved in Canada between 1991 and 1997 were determined to be breakthrough drugs by the criteria used by the Patented Medicines Review Board. Most were developed for commercial reasons but were not necessarily safer or more effective than existing drugs.[8]

- When a new medicine is introduced to treat a condition for which medication already exists, companies are not presently required to provide proof that the new medicine performs better, in terms of safety and efficacy, than existing ones. (They only need to show that new medicines are acceptably safe and more effective than a placebo, a pill with no active ingredient.) Health Canada should approach the ICH, ICDRA (International Conference on Drug Regulatory Authorities) and the WHO with a proposal to establish a comparative efficacy testing requirement for new drugs in order to increase the likelihood that new drugs are superior in some manner to ones already on the market (e.g.new drugs should represent better therapeutic alternatives than those already on the market, drug combinations should be avoided unless the combination showed a clear advantage as compared with that of each ingredient and there should be a clearcut medical need for any new product—these criteria were the ones that Norway used in its "medical need" clause until 1996 when it harmonised its approval criteria with those adopted by the EU.) Drugs should be tested not just against placebos, as is the norm, but also against appropriate existing drugs.

Companies are not required to direct a percentage of their research and development dollars to address identified but unmet patient needs.

- The drug industry cannot be relied on to research and produce pharmaceuticals that treat unmet medical needs. There has, for example, been very little drug company sponsored research into drugs to treat a variety of tropical diseases because, although many people are affected, companies don't stand to make sufficient profit from such medicines. The Canadian government, in alliance with other national governments, must become actively involved in supporting research and innovation in the interests of public health to meet the most pressing health needs.

## Opening the Doors to Public Consultation

The work of the ICH involves decisions that directly affect public health. While some proposed changes are positive, others – as this brochure has outlined – jeopardise public health and safety. To address these concerns, the ICH process should be much more accountable.

The ICH Steering Committee and working groups should have representatives from public health advocacy groups, developing nations, the generic drug industry, and the broader medical profession.

***Health Canada must make more efforts towards inclusion. ICH guidelines should not be adopted until after they have been reviewed and approved by a Canadian committee that includes members of all the relevant stakeholder groups.***

## Recommendations

Harmonisation of pharmaceutical regulation has important implications for public health, not just for the pharmaceutical marketplace. If public health were the priority, an International Conference on Harmonisation would differ substantially from the current ICH process. For a start, national governments and the WHO would be voting members, and the international and regional industry associations would be observers. Currently ICH operates in the opposite manner – it is chaired by the international brand-name industry association (IFPMA). The harmonisation should be reformulated into an open, accountable and democratic process.

Canada could play a truly visionary role by encouraging the WHO to set up a genuine democratic process relating to harmonisation and by demonstrating a willingness to help finance it.

Canada can additionally play a leadership role by ensuring that any discussions henceforth on harmonisation consider the specific implications for women's health as noted in this document. Canada has specific policies relating to a gender-based analysis of health policy (Women's Health Strategy, 1999) and guidelines for the inclusion of women in clinical trials (Inclusion of Women in Clinical Trials, 1997) which could be shared in the international arena.

**With these basic tenets in mind, we further recommend that:**

1. The House of Commons Standing Committee on Health as well as the Canadian Senate should conduct open, broad-based hearings on the effects on Canadians and Canadian health systems of international harmonisation of regulations relating to drugs and devices.

2. Women should be enrolled in clinical trials in all stages of drug development in Canada and elsewhere in numbers sufficient to be able to separately assess drug effectiveness, safety, side effects and dosage levels for women vs. men; results from male-only studies cannot be generalised to women. Government regulators, such as Health Canada, should ensure that adequate monitoring and enforcement of these guidelines takes place.

3. Only government regulators should be able to make exemptions in the exclusion of any populations in drug trials. This should not be left to the discretion of drug companies.

4. Health Canada should not adopt any ICH guidelines which reduce long term testing, or testing of two rodent species, unless there is unbiased and reliable scientific evidence that another model is equally valid.

5. Patient safety should be rigorously protected. Health Canada should ensure that a standard of 12 months toxicity testing in non-rodents is required prior to human testing and marketing approval, and should argue for the same standard in the international arena.

6. With respect to "Periodic Safety Update Reports" for new drugs, Health Canada should urge the ICH to harmonise these requirements upwards to the US standard of quarterly reporting to protect public health. Canada should follow the US model of standards for PSURs, and must additionally set up and fund an ongoing active post-market monitoring system that is at least as comprehensive as airline safety systems.

7. Determining what must be reported as "new information" of adverse drug reactions should not be left to the discretion of drug companies. Companies should report any patterns of Adverse Drug Events (any events that occur while a person is taking a drug whether or not they are thought to be associated with the product) and any other unexpected patterns to government regulators as quickly as possible.

8. Health Canada must have a policy and an effective warning system in place to let health professionals and the public know if a problem with safety or effectiveness of a drug is suspected or if a drug has been banned or restricted for safety reasons in other countries.

9. Health Canada should approach ICH, ICDRA and the WHO on how to address the neglect of standards for labelling and patient information, so that standards of best practice are adopted internationally (recognising that best practice standards may vary according to national cultures.) Priority needs to be given to clear labelling and informative patient inserts that take varying literacy levels into account. Labelling and inserts should insure that patients understand what they are taking, why, what side effects might occur and what to do if they are affected.

10. Health Canada should defend generic drug policies that protect consumers from rising prescription costs. Generic manufacturers should not be forced to adopt ICH standards that are inappropriate for them.

11. To ensure accountability, Health Canada should urge the Steering Committee and working groups of the ICH to have representatives from public health advocacy groups, developing nations, the generic drug industry, and the broader medical profession.

12. Before adopting ICH guidelines, members of all the relevant stakeholder groups noted above should be added to any Canadian committee which reviews these guidelines.

# References


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3. http://www.hc-sc.gc.ca/hpb-dgps/therapeut/htmleng/guide_ich.html
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5. **US guidelines:** "Guideline for the Study and Evaluation of Gender Differences in the Clinical Evaluation of Drugs" (FDA, 1993, http://www.fda.gov/cder/guidance/old036fn.pdf) and "Guidelines for the Inclusion of Women and Minorities in Clinical Research"(NIH, 2001, http://grants1.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm;
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   http://www.hc-sc.gc.ca/hpb-dgps/therapeut/zfiles/english/guides/clintrls/wominct_e.html
6. Heinrich J. Director Health Care-Public Health Issues. US General Accounting Office. Drug Safety: Most Drugs Withdrawn in Recent Years Had Greater Health Risks for Women. GAO-01-286R Drugs Withdrawn from Market. Letter to: To Harkin, OJ Snowe, US Senate and HA Waxman, House of Representatives. January 19, 2001
7. Reporting can be encouraged by making it clear to physicians that this is a valid and important activity (using Health Canada's usual vehicles for information communication) and by giving doctor's rapid and useful feedback about reports that they have filed.
8. For more on these topics, please see our brochures in this series: "How Safe are our Medicines" (2000), and "Direct-to-Consumer Prescription Drug Advertising" (2001).



**Women and Health Protection,** in collaboration with DES Action Canada, published this booklet to raise public awareness about the importance of public health principles of disease prevention.


**This publication** is one in a series that examines new debates related to health protection. Health Canada is currently modifying the federal health protection legislation that regulates medicines, food and harmful substances in the environment. The interests of the pharmaceutical and biotechnology industries, the food industry, the chemical industry and the nuclear industry are well represented in Ottawa, while ordinary citizens are virtually excluded from the development of health policies. Health protection for Canadians must be the legislation's first priority.

**DES (diethylstilbestrol) was one of Canada's worst drug disasters. Between 200,000 and 400,000 pregnant women and their children were unnecessarily exposed to a harmful medicine, with tragic results.**


DES was the first synthetic estrogen. The drug was prescribed to prevent miscarriage between 1941 and 1971 in North America (longer in Europe), but proved ineffective. Although good evidence from animal studies indicated that DES might cause cancer, the drug

- Was prescribed to millions of women worldwide.
- Continued to be used in pregnancy nearly 20 years after it was found to be ineffective.
- Was found to cause cancer in young women in 1971, thirty years after it was first prescribed.

**Written by**
members of Women and Health Protection, based on an original paper by John Abraham.

**The original idea for this series – Protecting Our Health – was conceived by**
Rosanna Baraldi, DES Action Canada.

**Other titles in this series include:**

*"How Safe Are Our Medicines? Monitoring the risks of drugs after they are approved for marketing"*

*"Direct-to-consumer Prescription Drug Advertising: When public health is no longer a priority"*

*"Preventing Disease: Are Pills the Answer?"*

For more information about **Women and Health Protection,** visit the website at http://www.whp-apsf.ca

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