The R_{XX} Factor: Different on the Outside. Different on the Inside? Rethinking the Medical Model and Clinical Trials

Kathleen Uhl*:

I have been asked to talk today about the Food and Drug Administration (FDA) and the issue of women in clinical drug studies, including the impact of having women in those studies. I will give you a perspective from the FDA and go over some of the regulations that govern women in clinical studies. I will end with some food for thought as to what it might mean, from a broader perspective, to include women in clinical trials.

First of all I just want to tell you what the FDA is. I give numerous presentations at medical organizations where there are a lot of physicians, pharmacists, nurses, et cetera, many of whom think they know what the FDA is. Yet I often find that they are not exactly sure what the FDA does. The FDA is a regulatory agency first and foremost. We are not a research agency like NIH, and so our mission and what is written in law is very different from other agencies in the federal government. We are the oldest consumer protection agency and we have oversight over a trillion dollars worth of commerce. On a daily basis that means about a quarter of every dollar you spend is something that the FDA is responsible for regulating. Basically, the FDA receives and reviews research information from companies who want to manufacture products. We oversee pharmaceuticals, whether they are prescription or over-the-counter; medical devices, whether it be a tongue depressor or an implantable defibrillator – the full spectrum. We regulate vaccines and blood products. We regulate food. Most of the food in this country is regulated by FDA, but not all. There are numerous agencies involved with regulating food, but to make it easy: we do not regulate meat. We regulate cosmetics. We regulate personal care products. We regulate veterinary products. Lastly, we do inspections, inspections at ports. You have heard a lot about those recently, especially with the recent peanut butter incident and salmonella in tomatoes and cilantro. Those inspections at ports and inspections of research facilities are conducted by the FDA should those facilities want to submit information for approval.

Why is it important that we are even talking about women in clinical studies? What does it matter? According to the Institute of Medicine, nine drugs were withdrawn from the market for safety reasons over a four year period. Many of these drugs had greater health risks in women and the top four of them had health risks specifically in women. In several other products, there were health risks in both men and women. However, in these specific incidences, it is just women who were harmed by the use of the products.

For example, there was a particular drug called Tedasmil that was taken to an advisory committee. These are large public meetings with experts brought in to hold a public discussion of the data. Tedasmil is basically used for what is called atrial fibrillation or atrial flutter. It is a rapid heart rate condition. There were similarities in how both men's and women's bodies handled this drug and the drug worked equally well in both sexes. The problem was that there were twice as many female deaths in these clinical studies. The question was then taken to the advisory committee. The committee was asked what it should do given that the drug worked for what it was intended to be approved for, but there were questions as to whether it should be allowed onto the market. The company proposed specific dosing that would be different for men and women, but the advisory committee members unanimously said, "no, do not approve this product." As a result, the product has not been approved by the agency. This was a huge blow to the company because it takes hundreds of millions of dollars to develop a product and the fact that there are differences between men and women has substantial economic implications.

In 1977 there was a regulation that the FDA put forward that actually excluded women from clinical studies and specifically excluded women of childbearing

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potential from early-phase clinical studies. The problem with that was it was overly-interpreted to mean women should be excluded from clinical studies and that all phases of drug development should exclude women. There are multiple phases of drug development. Although this is not the purpose of this talk, it suffices to say that some of the earliest studies are very small – ten, fifteen study participants – and what they basically do is slowly increase the dose to see if there are any adverse effects. They are not meant to show whether the drug works. That is the step where women were supposed to be excluded; not the large, multi-phase-, multi-center-, multi-country-, 4,000-participant studies. Excluding women right off the top actually violates some ethical principles. It violates the principle of autonomy and quashes the ability of a woman to make her own decision as to whether she wants to assume the risks and the benefits of participating in such a clinical study. Advocacy groups lobbied hard to have the regulation changed because it denied women access to some important and innovative therapies.

What followed in the seventies and the eighties was the HIV epidemic and the exclusion of much-needed, yet experimental, products for not just a life-threatening, but also a lethal medical problem. This issued forced a change in these regulations. In addition, advances in cancers and cancer therapeutics were also a large reason for advocacy groups to lobby to have the regulation changed. In 1993, this particular regulation was changed, but only via a guideline, which is much lower down the threshold of, "is this something that has to be done?" versus a more voluntary rule. Evidently the guideline did reverse the policy and required pharmaceutical companies to collect information about the participants in their studies. Companies were also required to analyze the data to look at effectiveness, whether there were particular adverse consequences, and pharmacokinetics, which basically gets to the bottom line of dosing.

In the early nineties, the thought was that if we were concerned about exposure to women of childbearing potential – and, hence, the developing fetus – that that concern could be taken care of with the use of appropriate language in the research protocol. Subsequently, the agency enacted a regulation in 1998 requiring companies to report in a submission with the data broken down by age, sex, and race. It does not necessarily say they have to analyze the studies based on those factors, but that the participants are spanning the spectrum of the demographics of the population. Another regulation that the agency has is the clinical hold rule. This regulation allows the FDA to stop a study if people are excluded from participation based upon their reproductive capabilities. It is not permissible to exclude women of childbearing potential or men because they could potentially impregnate a woman and the clinical study could be put on hold as a result of such exclusions.

There certainly are challenges to studying women. For one, women are harder to study. Women ask questions and do not just take things at face value. There are facilities that do clinical studies for the industry who do not want to include women because it takes too long to enroll them in studies because they ask so many questions. Women are less homogenous, meaning they are more difficult to analyze. If the argument is that we want to have women in the clinical studies, we need to understand whether we are talking about females in general or boys versus girls. There may not be that much different between a seven-year-old female and a seven-year-old male. In contrast, there is a huge difference between a 12 year-old female and a 12 year-old male. For example, whether females are within their reproductive potential or where they are in their monthly cycle are both dramatic physiologic changes that can impact a woman's response to a medication or contribute to the adverse effects she may experience. Pregnancy is a whole other matter. Further, there is the issue of whether someone is perimenopausal or postmenopausal. If you look at this as a continuum, it is not enough to just say 'women' in clinical studies.

Women are also expensive. The argument around expense is that you may have to drive up your sample size and enroll more people if you are forced to enroll a specific number of women. There is also the whole issue around hormones. Women will continue to menstruate, get pregnant, and become menopausal. These factors influence the conduct of clinical studies. Another challenge is the fear of liability. This is what drove the 1977 exclusion of women, specifically the birth defects associated with thalidomide. This is the most apparent teratogenic compound that exists. The fear of birth defects with pharmacologic agents is real and was the basis for exclusion for a long time. There were also key cases around DES and the Dalkon Shield that forced companies to be extremely cautious when enrolling women in subsequent studies.

Why are women not in clinical studies? To exclude women intentionally is not permissible, but women are often not recruited. Then there is the aspect of the large volumes of data. Despite the IT-friendly society that we live in and the advances in our health information infrastructure, we are still in the dark ages when it comes to data standards. By this I mean one data set, one clinical study, cannot necessarily be pooled with another clinical study because of how certain data is reported. I will give you one very simple example. The easiest example of a data point is what sex a person is. In a clinical study, what we want to see is every female and every male categorized the exact same way with the exact same nomenclature. So for a male, it always says, "M" and for a female it always says, "F" and for unknown or not registered it says, "U." That is not the way studies are conducted. Any symbol can be used. Since you cannot pool information across studies, it is hard to even know the extent of women's participation in studies.

Katie O'Callaghan*:

Like Kathleen, I am from FDA. She is from the Center for Drug Evaluation & Research (CDER); I am from the Center for Devices & Radiological Health (CDRH). My remarks today do not necessarily reflect the official views of the FDA. Today you have heard about some of the regulatory background, the difference between the guidelines, and what we have statutory authority as an agency to do. Why is there still a problem with the most recent regulation? Why are we still not getting enough information on women? I am going to talk about the problem, some solutions that are

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being discussed, and identify the key players in the game that need to work together to change the paradigm.

I really like the session title that we were assigned – *Different on the Outside. Different on the Inside?* It would seem you would assume that there are differences rather than assume that there are not. From a scientific perspective, that affects how you design your studies, how you design your devices, and even how you treat patients. If you come in with the assumption that there are differences, you are going to treat women differently than men as opposed to treating all patients the same. A lot of the medical field does not take this approach, especially with cardiovascular disease. Here are some general examples – not necessarily cardiovascular-specific – that clearly show there is something different on the inside because there are differences in disease. For osteoporosis, depression, or auto-immune diseases, there are differences in how things that we do affect our body and how that interplays with the development of disease; like the impact of smoking on health.

More women develop and die from heart disease than men. This is relatively new knowledge in the science and medical fields. Let us start with some observations. Look at what we know about the outcomes of heart disease: more women die of it, women are more likely to die from a heart attack, more women are likely to die from heart failure and after having a heart attack, more women are likely to have another heart attack. Even when women are treated, there may be differences in how well the treatment works in terms of effectiveness or the types of side effects or adverse events. Why is this? Specialists say it is because the difference with female patients is that they are older when they develop heart disease and they have more co-morbidities like diabetes or obesity. Why are women being diagnosed so late? Let us take a look at access. Some relatively recent studies have uncovered disparities in health care delivery for men and women with heart disease. Women are less likely to get an EKG, which is a standard diagnostic test for heart disease. Other diagnostic tests are often less accurate in detecting heart disease in women. Women are less likely to be referred to a heart disease specialist. When women do get treatment, they are less likely to get the right treatment, such as clot-busting drugs or catheterization procedures.

Why are women not getting the right treatment? As it turns out, we are still in the learning phases, from a scientific perspective, when it comes to the biology. There is a lot being uncovered, but we are still learning about the ways in which women and men are different, biologically speaking, in diseases that affect both. For things like breast cancer or pregnancy-related complications we have a relatively good understanding about how women and men are different. But for things like heart disease, we have just been treating males and females the same when, in fact, there may be male-typical heart disease with some variation and female-typical heart disease with some variation.

What about solutions? Let us start with educating women; patient awareness. The red dress campaign is one example. There is also the 'Go Red for Women' campaign. There is a lot of overlap and collaboration between the medical professional societies, NIH, patient advocacy groups, and there is outreach to female patients who have heart disease. Slowly but surely there has been a measurable increase in how much the public knows about heart disease in women.

As a result of education programs, more female patients know they are at risk for heart disease. What about the referral bias and the delivery disparity issues that we were talking about earlier? We do need to educate providers, but if there is a referral bias issue we cannot just talk to the cardiologists; we have got to go a step back. We need to talk to the primary care doctors, the ER doctors, or the OB/GYNs which, for many women, is their primary care physician. We need to go to the medical schools. The Association of American Medical Colleges has actually been looking at integrating more gender-specific teaching into their curriculum. A medical professional society has put out practice guidelines and there have been a few that have come out for treating and diagnosing women with heart disease.

The next issue is what to put in those guidelines. How should we be diagnosing and treating women with heart disease? We need to talk about research. What do we know about the biological reasons for sex differences, both in the healthy female versus the healthy male and then in men and women with heart disease, and then how they respond to the treatment? We need to analyze the trial data that we have in the drug, device, and treatment trials and look for and report any differences. When we try to do that, the statisticians say, "there are not enough women." The signals are still within the margin of error. We need to get more women involved. How do we do that? Patient awareness. At that point we have completed the circle. I am trying to paint a picture of how there are many components of this system that are all operating under the current paradigm. The regulation and policy issue is one aspect of it, but really it is going to require all of these pieces coming together. Who is responsible? In my opinion, all of the above: patients, primary care and specialist medical providers, the research industry who are designing the medical devices and drugs, the FDA, NIH, and the payors.

Our panel is also talking about rethinking medical models and clinical trials. The FDA is trying to change the paradigm by putting out a guideline for trials and marketing applications for medical devices. We are talking with the industry about enrollment targets to include more women in trials, evaluating data to identify what information should be released to the public and what necessitates further study, identifying barriers to women enrolling in studies, assessing at what point in the study are they dropping out, figuring out ways to minimize that, and studying other systematic changes. We need more data about sex-based differences and this will come about with an FDA-industry partnership, through the NIH's work with academia to conduct studies, incentives from CMS and the other insurance providers, and practice guidelines from medical professional societies.

Rebecca Wolf*:

I will be discussing a two-part article about personalized medicine which I co-authored with Professor Corrine Parver, several other WCL students,

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and health law practitioners. I will be touching on a few of the pertinent health law issues addressed in these publications. I will be explaining the new technology of pharmacogenomics (juxtaposed against traditional model of one-size-fits-all medicine) which was made possible, in part, by the Human Genome Project that was completed in 2003. I will be discussing the benefits and concerns associated with personalized medicine, namely the exacerbation of gender inequities in clinical trials and concerns about genetic-based discrimination. In that vein, I will be describing some of the legal provisions which can protect individuals from genetic discrimination. Finally, I will conclude that pharmacogenomics is a promising new field of medical research which has the potential to revolutionize the field of medicine. However, it is important to consider and address gender inequities and clinical trials. In addition, potential genetic discrimination means that there is a need for scrupulous legal protection.

One-size-fits-all medicine is when the general population receives essentially the same treatment for a particular disease. The only tailoring that occurs is for adults, children, and the elderly. One-size-fits-all medicine does not provide additional information about how an individual patient will react to a particular type of treatment or what type of dosage would be beneficial given that patient's rate of drug metabolism. Two benefits of one-size-fits-all medicine are as follows: first, one-size-fits-all medicine is less costly in the short term than tailoring treatments for each individual patient; second, standardized treatment simplifies interventions.

However, there are many concerns associated with one-size-fits-all medicine. First, individual differences and drug metabolism can result in ineffective treatment or a drug overdose, in some patients. Second, ignoring genetic differences can result in serious side effects. In fact, only one-third of all drugs act as expected when prescribed. For instance, in the treatment of asthma, the same drug can provide relief for one patient and have serious side effects for another. In a heterogeneous population, such as in the United States, there will be less predictability of reaction to treatment due to a diverse gene pool.

Pharmacogenomics, or personalized medicine, is an alternative to one-size-fits-all medicine. It was made possible, in part, by the Human Genome Project. The Human Genome Project was an effort to decode the sequence of DNA and map the entire human genome. The Human Genome Project may ultimately give medical providers information about an individual's predisposition to developing a particular disease or the way in which an individual will react to a certain type of medical treatment. Personalized medicine is the marriage of genomic technologies and pharmaceuticals. The primary purpose of personalized medicine is to individualize medical treatment for each patient's DNA.

Unlike one-size-fits-all medicine, personalized medicine is much more likely to be beneficial and safe for a particular patient because a physician prescribes a particular drug and dosage based upon the individual's genotype. There are several benefits of personalized medicine. First, there is a potential for more effective treatments for each individual. Second, physicians may intervene at an earlier stage of a disease or even before a disease manifests based upon knowledge of a patient's predispositions. Third, personalized medicine may help researchers identify disease targets, speed clinical trials, and advance treatments for specific populations. However, as with any new technology, there are also associated concerns. Two concerns that I will be discussing are that personalized medicine could exacerbate gender inequities in medicine and that individuals will experience discrimination based upon their genetic information.

There is a historical lack of inclusion of women in medical research. Until the late 1980s, women were excluded from participating in clinical trials through explicit policies, practices, and severe neglect. In 1993, the NIH Revitalization Act required the inclusion of women in clinical studies, as well as the analysis of research results by gender. Now, more than fifteen years later, despite the NIH Revitalization Act, women remain excluded from clinical trials. As you can imagine, if women are excluded from clinical trials related to personalized medicine, then there will be a paucity of information about how to treat women on an individual basis.

In addition to exacerbating gender inequities, there is a concern that individuals will experience discrimination based upon their genetic information. Genetic discrimination occurs when people are treated unfairly because of differences in their DNA that increase their chances of getting a certain disease. For example, a health insurer might refuse to give coverage to a woman who has a genetic predisposition for breast cancer. Employers also could use DNA information to decide whether to hire or fire workers. This is particularly troubling in the current economic climate in which companies are trying to save money. To employers, it might be more cost-effective to employ someone who is not predisposed to a costly disease.

There are several existing legal protections against genetic discrimination. Title VII of the Civil Rights Act of 1964 prohibits all private employers with fifteen or more workers; labor organizations; employment agencies and federal, state and municipal government employers from discrimination on the basis of race, color, religion, sex or national origin. The statute does not specifically address discrimination based upon genetic information but Title VII may protect against discrimination on the basis of an individual's genetic makeup if that discrimination disproportionately impacts individuals belonging to a protected class. The Americans with Disabilities Act (ADA) prohibits discrimination in employment, public services, public accommodations and communication against individuals with disabilities. In March 1995, the Equal Employment Opportunities Commission issued an interpretation of the ADA that states: "[e]ntities that discriminate on the basis of genetic predisposition are regarding the individuals as having impairments and such individuals are covered by the ADA." However, because interpretation has not yet been tested in the legal arena, it remains an interpretative policy guideline.

The Health Insurance Portability and Accountability Act, or HIPAA, ensures that individuals who change health coverage are not denied or restricted in employment-related coverage on the basis of a preexisting condition. HIPAA was the first federal law to address the use of genetic information in the health insurance context. It prohibits group health plans and group health insurers from excluded individuals from coverage on the basis of genetic information unless there is an actual diagnosis of the condition related to the genetic information. In 2000, President Clinton signed an executive order prohibiting every federal department and agency from using genetic information in any hiring or promotion action.

Finally, and most recently, the Genetic Information Nondiscrimination Act (GINA) of 2008 prohibits the improper use of genetic information in

health insurance and employment. The Act prohibits group health plans and health insurers from denying coverage to a healthy individual or charging that person higher premiums based solely on a genetic predisposition to developing a disease in the future. It also bars employers from using individuals' genetic information when making hiring, firing, and job placement or promotion decisions.

In conclusion, pharmacogenomics is a promising new field of research which has the potential to revolutionize medicine as we know it. However, it is important to consider and address gender inequities in clinical trials. In addition, potential discrimination based upon genetic information means that there is a need for scrupulous legal protections.

Audience Question:

Is there anything happening now to address the refusal to include women in clinical trials? Will it be just the same kind of situation but with a new dynamic with pharmacogenomics or, in fact, will we resolve it? There seems to be a real opportunity for personalized medicine to exclude half of the country. Is something being done?

Kathleen Uhl:

It is interesting that you bring that question up because there are certainly genomic databases that exist and it is not that surprising that some of the data does not include information about sex. A large database of information on multiple patients with no information on their sex is not going to answer any of the questions that you have raised. It comes back to the issue of data standards. What are the standards that need to be collected for every patient, not just in research but at every clinical encounter? How do we develop a systematized manner of collecting health information so that a patient's sex is collected every time? That question is actually addressed through the health IT aspect of the stimulus package. Health IT is important, not just for the patients' electronic medical record with his or her practitioner, but also the accessibility of that record. Someone entering medical data in Washington, D.C. or Portland, Oregon will complete all the same fields for every encounter. That is still in the works. There are certainly systems that use electronic health records but yet there is no universal electronic health record.

Katie O'Callaghan:

Health IT has been getting a lot of attention as part of an overall health reform. It has potential to be part of the solution, because when everything is electronic, it may be easier to standardize data or at least access data. Often, for the data we receive at the agency level, it would be really burdensome to go back to the actual patient-level data and determine whether the patient was male or female. With electronic records it becomes much more accessible. There's also a Heart Act for Women which passed last year in the House and did not make it through the Senate, but is being reintroduced. The Agency for Healthcare Research and Quality, which creates disparities reports, would be charged with doing women-specific reports by utilizing information from various databases, nationwide information resources, and certainly anything that would become available via a health IT initiative.

Kathleen Uhl:

I want to comment about the use of the terminology 'excluded' versus 'not included', because they mean two different things. Women can be intentionally excluded from participation in studies, like they were in the 1970s. They were not allowed to participate in studies: totally excluded. In today's situation, and using cardiovascular health as an example, women are not included in the studies to the same extent that men are. They certainly are included. There are some great meta-analyses in medical literature that assess women's participation in large, multicenter cardiovascular studies and for drugs and devices. Women represent twenty to thirty percent of participants. Women are not expressly excluded but if the enrollment criteria states that participants must be under age sixty five, fewer women will be included, because they tend to develop heart disease at an older age than men.

It is a subtlety to say that, but there are people who would take exception to anyone saying women are excluded from studies because there is policy, regulation, and law that prohibits the exclusion of women from studies.

Katie O'Callaghan:

The other piece, as far as the genomics and personalized medicine go, is that there have been an increasing number of reports from the basic science research field finding that the receptor associated with this marker for heart disease is much more prevalent in women than in men. I think the more we start to learn about the genetic predisposition to disease, the more that may come into play.

Audience Question:

Last February, the Supreme Court ruled on a case that gave a huge amount of deferential authority to the FDA. Specifically, if something is reviewed and approved by the FDA then, even if it is defective and hurts somebody, they cannot bring a lawsuit. Now, I just wanted to know what your opinion of that is because what happens if there is another *Dalkon Shield* or DES case? Somebody who is injured by that cannot bring a lawsuit. I want to know what their remedy is. They cannot go to the court, they cannot get any relief or remedy for that or prevent this from happening again, and I wanted to know what your opinions were on that decision.

Katie O'Callaghan:

I do not know all the legal specifics of the court case from reading the news reports. I believe that the decision, in regards to preemption, is about not suing the company if the device or drug was used exactly as the label was written by the FDA for the approved use in patients. The issue with FDA trials and off-label marketing or usage of treatment is that the studies that FDA receives, reviews, and evaluates the treatment on are very specific and, oftentimes physicians use them in areas that are not studied. In those cases, I do not think that preemption would rule out medical malpractice suits. So if you are harmed as a result of off-label usage of a device, drug, or a biologic by your physician, medical malpractice is still not ruled out by preemption.

Moderator:

Dr. Uhl, you talked about the differences among women and how that creates a difficulty in women being part of clinical trials. I was wondering if you had any thoughts about how to address those differences to make it possible for women to be part of those clinical trials in a real, concrete way.

Kathleen Uhl:

Well, the reason I discussed that was two-fold: one, to let people see some of the barriers and two, to emphasize the heterogeneity of the female population. That is more the food-for-thought part of the talk. It is what we need to think about it if the game plan is to increase participation of women in studies and specifically, find out how applicable the data is to the entire female population? So, if we are just studying women who are under forty-five in a particular area, but there are women in their seventies or eighties that will be taking or using this same medical product, how applicable is that data? I do not have the answer to that, but I think that the way to answer those questions is probably not in the context of pharmaceutical or device-sponsored studies because, if that is the expectation, we will not see any new medical products on the market. If the expectation is, as Katie alluded to, some of these large claims databases that AHRQ, theAgency for Healthcare Research and Quality, or CMS have access to, then we will be able to better address the effects from medical product use, whether they are efficacy or safety, in different populations of women.

I also put it there to show that there will always be excuses as to why we do not study more women. If you want to counter them you have to know what they are in the first place and why people feel that way. Then you can go to the next step and say, "how do we improve the recruitment of women in clinical studies?" That is an entirely different focus that requires the next question to be "how do you promote recruitment and retention of women in clinical studies?"

Katie O'Callaghan:

As far as cardiovascular trials, the agency had a public workshop – two, actually; one in June and one in December – specifically looking at that. We got together a group of physicians via professional societies, patient advocacy groups, and several of the agencies under HHS: FDA, NIH, CMS, and AHRQ. When you look at anything, be it heart disease or prevention or any type of access to the healthcare system, there are a lot of disparities in women and men accessing healthcare. Then there are separate disease-specific or product-area-specific issues. For example, with heart disease, one thing that I learned from a think tank relates to body image and cultural issues. An ER doctor had mentioned that one of the reasons why he thought women might be less likely to get the EKG is because in a crowded ER, when you do not have a room available, a guy who has chest pain is comfortable with tearing his shirt off and strapping on all the electrodes for the EKG. If a woman has mild chest pain and is short of breath, she may not want to tear her shirt off. She is still fully cognizant. She is not falling on the ground and she does not necessarily know it is a heart attack. She is probably going to wait for the room. There are disease-specific issues but it is really very multifaceted and it is going to take collaboration from all the stakeholders to figure out what is needed for each specific area.

Kathleen Uhl:

The heterogeneous population of women has different requirements if you want them in clinical studies. For example, if you want to recruit women into a clinical study who are twenty to forty years old and have kids, unique issues arise. How are you going to get her into your clinical study? You have to provide childcare at the site of the clinical study. You probably have to provide transportation. For the aging female population, as shown by information presented earlier today talking about salary and income, older women are living below the poverty line. If you want to enroll older women, they are more likely to have a need for bus fare or cab fare to get to the site of the study. There is not a cookie-cutter approach to participant enrollment, yet this is the paradigm that has been followed in the research community.

Audience Question:

My question is about issues that are only related to women; namely, reproductive health. What is going on with the trials there? I know there were a lot of issues when birth control first came out and there are some moral/ethical dilemmas with those trials.

Kathleen Uhl:

It depends in which area you are referring. For example, there are a lot of studies ongoing for osteoporosis. Since there is certainly a great market for contraception, companies are still creating new contraceptives; whether they are drugs or devices or drug/device combinations.

The area of pregnancy is where there is really a dearth of information because of the liability aspect. We know pregnant women get sick. We know pregnant women need medical treatment. Whether they need diagnostic tests, they need treatment with medication or treatment with medical devices. The community of clinicians and the developers of these products are scared to death to touch pregnancy because of liability. There are very few products under development for use during pregnancy. There may be more in the medical device area because of use in labor and delivery, but when it comes to medication, there is a dearth of studies to collect that. We know women take medication when pregnant. There have actually been numerous workshops to discuss this and ask questions like "is it ethical to study the use of medical products in pregnancy?" The counter is, it is unethical not to. If the standard of care is to use this particular drug for a patient with asthma when pregnant, then how is it unethical to study the outcomes in the woman or in her developing fetus from that exposure? Though the ethics around it are substantial, the medical liability part is even larger. I think the other part around pregnancy is that it is a limited-term medical condition where the end result, in the majority of circumstances, is a healthy baby. The issues around pregnancy tend not to be embraced as much by the women's health advocacy community.