

**Consensus Conference on Systemic Autoimmune Rheumatic Diseases (SARD):  
A Research Forum on Lupus, Scleroderma, Sjögren's Syndrome,  
Autoimmune Myositis and Vasculitis  
December 2 – 4, 2005, Toronto, Ontario, Canada**

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## **Consensus Conference on Systemic Autoimmune Rheumatic Diseases (SARD): A Research Forum on Lupus, Scleroderma, Sjögren's Syndrome, Autoimmune Myositis and Vasculitis**

### **Executive Summary**

In December 2005, a group of internationally renowned scientists and clinicians met in Toronto to share information about Systemic Autoimmune Rheumatic Diseases (SARD). These potentially serious but less well-known diseases are related to arthritis; they include systemic lupus erythematosus (SLE), scleroderma, Sjögren's syndrome, myositis and vasculitis.

The goals of the meeting were to educate stakeholders on the scope of current research; to develop the Canadian research agenda in SARD; to find ways of encouraging scientists, research funding agencies, government, industry and professional organizations to work together; to create an opportunity for patients to participate in setting the research agenda; and eventually, to make new discoveries about causes, prevention, diagnosis, treatment and management of SARD.

Approximately 100 participants including clinicians, basic scientists, health policy makers, trainees and patient/consumer advocates attended the two-day conference. They learned that SARD are much more common in women than in men, and also that people of aboriginal, African and Asian descent are somehow more susceptible. Because SARD is a concern in aboriginal populations, a number of aboriginal health care experts and consumers attended the conference.

The first day of the conference was devoted to providing education and assistance for the SARD patients and consumers who attended. Through this session, they were equipped and encouraged to become active participants in the subsequent scientific portion of the meeting.

Over the following two days, approximately a dozen scientists presented the latest information about SARD. Topics included: the epidemiology of SARD, including how these diseases affect minority groups; pathophysiology, genetics and environmental factors in SARD; lessons learned from past research, including experience from Germany and the U.S.; new approaches in diagnostics; and elements of designer therapeutics for SARD.

Between scientific presentations, participants engaged in small group exercises designed to identify challenges, build consensus and broadly outline a new research agenda for SARD in Canada. They agreed that the following obstacles exist and must be addressed:

- There are limited financial incentives for researchers or industry to do research on these comparatively rare conditions.
- There's a lack of funding to support and sustain research infrastructure.
- SARD research is by nature multi-disciplinary and multi-institutional, and this makes it expensive.
- There is a chronic shortage of expert researchers and support staff.

- The effective exchange of information about SARD is hampered by the lack of an official communication system for sharing, especially between basic and clinical researchers.
- Patients and family members need to be more actively involved and supported in determining the research agenda and in helping set priorities.

Following the Consensus Conference, a SARD Working Group met to consider all the small group reports and recommendations. They agreed on the following key points:

- There are unique, unmet needs associated with SARD.
- Barriers exist which prevent us from meeting these needs.
- To make progress, we must assert and follow Strategic Directions.

The Working Group has developed and will continue to refine a “SARD Action Plan” which will focus existing and new activities over the next six to nine months. Work should move forward in the context of three “priority themes”:

**Treatment** Treating patients is important. Steps must be taken to ensure that new treatments are moved rapidly from the laboratory to the market and tested following the best clinical research practices. It is also vital to streamline the current system so patients are referred to the appropriate specialists for optimal treatment in a timely manner.

**Research** This is a critical if we are to obtain a better understanding of SARD and thus improve patient care.

**Collaboration** Efforts must be made to coordinate the activities of basic and clinical scientists, other academics, health care and support organizations and patients to ensure the best possible outcomes for those with SARD.

# **Consensus Conference on Systemic Autoimmune Rheumatic Diseases (SARD): A Research Forum on Lupus, Scleroderma, Sjögren's Syndrome, Autoimmune Myositis and Vasculitis**

## **Introduction**

In December 2005, a group of internationally renowned scientists and clinicians from Europe, the United States and Canada met in Toronto to share information about Systemic Autoimmune Rheumatic Diseases (SARD). These potentially serious but less well-known diseases related to arthritis include systemic lupus erythematosus, scleroderma, Sjögren's syndrome, myositis and vasculitis.

Approximately 100 participants including clinicians, basic scientists, trainees, health policy makers and patient/consumer advocates attended the two-day conference. Special invitations were sent to people living with a diagnosis of lupus, scleroderma or Sjögren's syndrome, and 20 patient/consumer invitees took part, sharing their experiences and concerns. Many represented non-profit organizations such as the Canadian Arthritis Network, the Arthritis Society, Lupus Canada, the Scleroderma Society of Canada and the Sjogren's Syndrome Association.

The goal of this meeting was to promote and strengthen a SARD research agenda and, eventually, to make new discoveries about causes, prevention, diagnosis, treatment and management.

No reliable data exist about how many Canadians have been or will be diagnosed with each of these conditions. But people of all ages and from all walks of life are affected, often during their most productive years. SARD patients must cope with pain and fatigue every day and may develop serious health problems which can significantly shorten their lives.

There is evidence that SARD are much more common in women than in men, and also that people of aboriginal, African and Asian descent are somehow more susceptible. Because SARD is a concern in aboriginal populations, a number of aboriginal health care experts and consumers attended the conference which was sponsored in part by the Institute of Aboriginal Peoples' Health (part of the Canadian Institutes of Health Research or CIHR).

The main goals of the SARD conference were:

- to educate stakeholders on the scope of current research – in Canada and around the world – and also to develop the Canadian research agenda in SARD
- to find ways of encouraging scientists, research funding agencies, government, industry, professional organizations and patients to work together towards a better understanding of SARD and possibly to improved diagnosis and management
- to create an opportunity for patients to participate in setting the research agenda

Highlights from the Scientific Presentations and a set of Recommendations and Next Steps (based on the group discussions over the three-day conference) are presented here.

## The incidence and prevalence of SARD (U.S. data)

	Annual incidence per 100,000	Prevalence per 100,000	Percent female	Median age
<b>Rheumatoid arthritis</b>	24	860	75%	58
<b>Lupus (SLE)</b>	7	24	88%	40
<b>Sjögren's syndrome</b>	4	14	94%	59
<b>Polymyositis</b>	2	5	67%	52
<b>Systemic vasculitis</b>	2	15	43%	63

adapted from DL Jacobson et al, *Clin Immunol Immunopath* 1997;84:223-43

### About Systemic Autoimmune Rheumatic Diseases (SARD)

**Lupus** is the name given to several related diseases. The most common and serious type is called *systemic lupus erythematosus* or SLE. In SLE, the immune system attacks healthy tissues, including the skin, muscles and joints, causing them to become swollen and painful. The heart, lungs, kidneys, blood vessels and the nervous system can also be affected. There may be periods of inflammation, called flare-ups, and then periods where there is little or no inflammation which are called remissions. Women develop lupus up to ten times more often than men – most often between ages 15 and 45.

**Scleroderma** This is a condition characterized by a hardening and thickening of the skin and other tissues. There are two main types of scleroderma. *Localized scleroderma* affects mainly the skin but can also involve the muscles and joints. *Generalized scleroderma* affects the skin as well as the internal organs, such as the heart, lungs and kidneys. Less visible changes include damage to the cells lining the walls of small blood vessels. Women develop scleroderma up to five times more often than men. The disease usually appears in people between the ages of 30 and 50.

**Sjögren's Syndrome** This chronic disorder is characterized by damage to the salivary, tear and mucous-secreting glands, resulting in dry eyes (xerophthalmia) and/or dry mouth (xerostomia). The disease can also affect other parts of the body including joints, muscles and nerves, organs such as the lungs, kidneys, liver, pancreas, stomach and brain, or glands such as the thyroid gland. Ninety percent of those diagnosed are women, most often after age 45. About half the people diagnosed with Sjögren's syndrome also have other rheumatic conditions like rheumatoid arthritis, lupus, scleroderma or polymyositis

**Myositis** Polymyositis is a disease that causes muscles in any part of the body to become weak. This weakening can also affect the lungs and the heart. The disease is called *dermatomyositis* when the patient's skin is also affected. Polymyositis and dermatomyositis can occur at any age but are most common in children aged five to 15 and in adults over age 50. Women are affected by polymyositis and dermatomyositis twice as often as men.

**Vasculitis** This is a systemic autoimmune disease of blood vessels that can affect many parts of the body. In general, the blood vessels become inflamed, causing a variety of symptoms and damaging certain organs over time. There are many kinds of vasculitis, including *Giant Cell Arteritis* (affecting blood vessels supplying the head and neck); *Wegener's granulomatosis* (frequently involving the kidneys, the lungs, and – almost always – the upper respiratory tract); and *Buerger's disease* (involving the fingers and toes).

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**Consumer Orientation Session  
Friday, December 2, 2005**

The first day of the conference was devoted to providing education and assistance for the SARD patients/consumers who attended. "The purpose was to help us all become active participants in the subsequent scientific portion of the meeting," says Robert Buzza of Vancouver, B.C. who was there in his role as President of the Scleroderma Society of Canada.

"We think it's promising that the Institute of Musculoskeletal Health and Arthritis, the Institute of Infection and Immunity, the Institute of Gender and Health, and the Institute of Aboriginal Peoples' Health were among the 16 conference sponsors," he adds. "We hope that support for this major autoimmune conference will eventually result in grant applications leading to significant funding for research into diseases such as scleroderma."

Between scientific presentations, the consumer participants took part in small group exercises. These activities were carefully designed to identify challenges, build consensus and broadly outline a new research agenda for SARD in Canada.

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**Scientific Presentations  
Saturday, December 3, 2005**

**Where Are We? Where Are We Going?**

*Dr. Bhagirath Singh, Scientific Director of the CIHR Institute of Infection and Immunity and Professor in Microbiology and Immunology at the University of Western Ontario.*

Autoimmune disease is a major health burden affecting between five and seven percent of the population or about 1.5 million Canadians, the majority of them female.

The immune system plays a key role in the disease process, and there are strong genetic and environmental components that must be considered as well. Studies of specific autoimmune diseases, including Systemic Autoimmune Rheumatic Diseases (SARD), may provide new and additional insights into the pathogenesis of autoimmune diseases affecting other organ systems.

Currently, about five percent of the Canadian Institute of Health Research (CIHR) budget is spent on autoimmune research, and this amount is steadily increasing. This funding – about \$35 million annually – is distributed among the 13 CIHR Institutes to study various autoimmune diseases.

The CIHR Institute of Infection and Immunity has a mandate to support research that enhances immune-mediated health to reduce the burden of infectious disease, immune-mediated disease, and allergy through prevention strategies, screening, diagnosis, treatment, support systems and palliation.

For this reason, the Institute of Infection and Immunity, in collaboration with partners including other CIHR Institutes, launched a request for applications in December 2005 entitled “New Emerging Team Grants - Clinical Autoimmunity.” We expect that this investment – at least \$10 million over five years – will fund at least four research teams in the area of clinical autoimmunity.

Some questions of interest include:

- What influence does genetics have on autoimmune disease expression and progression?
- What happens to the immune system during the progression of a specific autoimmune disease?
- What role if any do infectious agents play in autoimmune diseases?
- How does the immune system function in animal models?
- What effects do various therapeutic interventions have on the immune systems of patients with autoimmune disease?
- What can we learn about social and epidemiological factors in autoimmune diseases?

The research which flows from this initiative will potentially have an impact on SARD. These efforts will likely benefit from integration, teamwork and focus, especially if the goal is to make a positive impact on health outcomes.

## The Epidemiology of SARD

*Dr. Sherine Gabriel* Chair of the Department of Health Sciences Research at the Mayo Clinic and Professor of Epidemiology and Medicine at the Mayo Clinic College of Medicine in Rochester, Minnesota

Epidemiologic studies include simple descriptions of the manner in which disease appears in a population (i.e., levels of disease frequency; incidence and prevalence; mortality; trends over time; geographic distributions; and clinical characteristics) and studies that attempt to quantify the role of putative risk factors for disease occurrence.

Incidence studies include all new cases of a specified condition arising in a defined population, while prevalence studies include all cases with the condition that are present in a population at a particular point in time.

Each of the five diseases under discussion – systemic lupus erythematosus (SLE), scleroderma, Sjögren's syndrome, myositis and vasculitis – is relatively rare, but as a group, SARD are fairly common. The diseases are of great interest to epidemiologists who are seeking descriptive information and are also undertaking risk factor analyses.

Researchers are beginning to view SARD as a class of disorders, an approach which has been extremely rewarding in cancer research. The evidence so far suggests they are complex, overlapping disorders with a complicated etiopathogenesis.

Known risk factors to date include genetics, hormonal factors, lifestyle factors (like diet, smoking history) and infectious agents. In most SARD, incidence increases with age, and there are known geographic, temporal and seasonal variations. Comorbidities are also common.

The following conclusions are based on a review of data on the descriptive epidemiology (incidence, prevalence, and survival), and risk factors associated with the following systemic autoimmune diseases:

**Giant Cell Arteritis (GCA)** This type of vasculitis may hold clues to causes and potential treatments for SARD. It was first recognized as a systemic vascular disease in 1941 and, until recently, has been considered rare. It is now known to be an important cause of morbidity in the elderly, and epidemiologists predict that disease burden for GCA will increase as the population ages. There is evidence that GCA varies widely by geographic region. For example, it is more common in Scandinavia (27/100,000) and the northern U.S. (19/100,000) compared to southern Europe, and the southern U.S. (7/100,000). This suggests a genetic disposition to GCA or some common exposure. Some epidemiological evidence points to infectious trigger in a genetically susceptible host.

**Systemic Lupus Erythematosus (SLE)** This is a rare autoimmune disease affecting primarily young women. Signs and symptoms overlap with rheumatoid arthritis (RA).

We recently reported the incidence and mortality of this disease in a geographically-defined population over a 42-year period. These results indicated that, over the past four decades, the incidence of SLE has tripled. The average incidence rate (age- and sex-adjusted to the 1970 U.S. white population) was 5.56 per 100,000 (95% CI: 3.93-7.19) in the 1980-1992 period, compared with an incidence of 1.51 (95% CI: 0.85-2.17) in the 1950-1979 period.

The reported prevalence of SLE has varied significantly. We reported an age- and sex-adjusted prevalence as of January 1, 1992 at approximately 1.22 per 1,000 (95% CI: 0.97-1.47). This prevalence is higher than most other reported prevalence rates in the continental U.S., which have ranged between 0.146 and 1.24 per 1,000.

Our data also show that the survival rate for individuals with SLE (while still poorer than expected for the general, non-affected population) has improved significantly. It is possible that increases in incidence and a decrease in mortality may be related to improved ascertainment of mild disease.

**Sjögren's syndrome** Few studies have been done to describe the epidemiology of Sjogren's syndrome and keratoconjunctivitis sicca. The prevalence of dry eyes or dry mouth and of primary Sjögren's syndrome among 52- to 72-year old residents of Malmö, Sweden (according to the Copenhagen criteria), were established in 705 randomly selected subjects who answered a simple questionnaire. The calculated prevalence in the population was 14.9 per cent for keratoconjunctivitis sicca (95% CI: 7.3-22.2); 5.5 per cent (3.0-7.9 for xerostomia; and 2.7 per cent (1.0-4.5) for autoimmune sialoadenitis and primary Sjogren's syndrome.

In a Danish study, the frequency of keratoconjunctivitis sicca in persons age 30 to 60 years was estimated at 11 per cent (according to the Copenhagen criteria); the frequency of Sjögren's syndrome in the same age group was estimated to be between 0.2 and 0.8 per cent.

There have been reports associating Sjögren's syndrome with other rheumatic and autoimmune conditions, including fibromyalgia, autoimmune thyroid disease, multiple sclerosis, and spondyloarthropathy.

## SARD in Minority Groups

**Dr. Christine Peschken** Assistant Professor at the University of Manitoba and rheumatologist/researcher at the Health Sciences Centre and St. Boniface General Hospital, Winnipeg, Manitoba

There is reasonable evidence that in Canada, SARD is more common among aboriginal peoples (First Nations, Metis, Inuit) and also among those of Asian descent (Chinese, South Asian, South East Asian) than it is among Caucasians, for example. The rate of growth in these two groups is increasing at about six times the rate for the rest of Canada's population.

However, there is growing recognition that a variable phenotype exists in individuals from different ethnicities. These disparities probably arise from the interaction between genetic and non-genetic factors including environmental exposures. It's likely that socioeconomic, demographic, cultural and behavioural components also play some role.

Many scientists are looking at prevalence data in various ethnic groups as a way to design research studies into the etiology of autoimmune rheumatic diseases. For example:

- While there are no Canadian estimates on the prevalence of systemic lupus erythematosus (SLE), it is thought that the frequency is somewhere between 50-150/100,000. Among the Algonkian Indians in Manitoba, the prevalence of lupus was found to be twice that of the non-Indian population; in the Nuu-Chah-Nulth on Vancouver Island, the prevalence was between 300-500 per 100,000. However, a low prevalence of lupus was found among the Inuit people in Keewatin (in the Northwest Territories).
- There's evidence that aboriginal patients with lupus are more likely to die from their disease compared to Caucasian patients. However, this isn't true for Asians with lupus – a finding which may be explained by socioeconomic factors and which may provide clues about cause and prevention.
- British data suggest that SLE is twice as common among those of Asian ancestry compared to Caucasians. While no good data exist in Canada, there is an "over-representation" of Asians in most Canadian lupus cohorts. British studies have found prevalence rates of 48.8 cases of SLE per 100,000 in people of Asian ancestry compared to 20.3 cases per 100,000 in those of Caucasian descent.

Researchers who study links between ethnicity and SARD must proceed cautiously. There are marked "within-ethnic" differences in the frequency and natural history of SLE. One problem facing researchers is that self-reported ethnicity is an imprecise way of capturing genetic contribution to disease. Environmental, socioeconomic and genetic variables are all confounded to some extent in genetic studies of SARD.

There is much potential in studying specific ethnic groups known to be at greater risk for SARD. For example, it would be possible to conduct family studies within a relatively homogenous ethnic group. Or one might study differences in disease incidence and severity among aboriginal Canadians living in cities vs. those living on First Nations' reserves. Researchers could compare the impact of these autoimmune diseases on Asians born in Canada vs. those born in China, Japan and areas of Southeast Asia.

However, researchers interested in conducting SARD research within aboriginal communities must pay attention to issues of trust and community consent. Aboriginal communities are often geographically isolated; they also have common histories and traditions that make them distinct from the dominant culture and political sovereignty. "The emphasis on individual rights in contemporary research ethics often fails to take into account important relationships of community," Dr. Peschken said, quoting from a paper on research ethics in First Nations health research.

With respect to doing genetic research on SARD in aboriginal communities, the group's collective autonomy is challenged if researchers, with the informed consent of only a few individuals in the group, can probe for information about the whole group (Greely, 1997:1431). The overall goal should be to develop the capacity of aboriginal people to assume greater control for research conducted for and by Canadian aboriginals. This means exposing native communities to research methods and results, increasing their awareness, and assisting them in setting their own research priorities.

Similarly, cultural awareness and community consent will also be important when working with other ethnic groups.

## **What Have We Learned About the Pathophysiology of SARD?**

*Dr. Mary Crow, Senior Scientist and Associate Chief for Rheumatology Research at Hospital for Special Surgery in New York; Professor of Medicine and Immunology at Weill Medical College of Cornell University, New York City, N.Y.*

The immune system is complex and so are SARD. Indeed, each of these different diseases has its unique features and involves distinct immune mechanisms. But through careful study of both common and distinct features of SARD, scientists are developing a new understanding of triggers, genetics and immunological alterations that may lead to pre-clinical interventions and disease prevention.

Possible viral triggers for Sjögren's syndrome and systemic lupus erythematosus (SLE) are being explored. For Sjögren's syndrome, triggers under scrutiny include the Coxsackie virus and the Epstein-Barr virus. For SLE, scientists are looking at Epstein-Barr or some kind of retrovirus.

Recent studies have found that it is possible to detect specific autoantibodies in the blood of apparently healthy people many years before they are diagnosed with SLE. Other research has found high levels of plaque in the arteries of patients with SLE, even though they show no other signs of cardiovascular disease.

Scientists interested in the pathophysiology of SARD are taking a two-pronged approach to the puzzle of autoimmune rheumatic diseases. This means considering both beneficial and harmful immune responses. The body has both innate and adaptive immune responses which may be beneficial or harmful, depending on a host of factors. We need to understand how such responses might contribute to the development of these complex disorders.

## Genetics and SARD

**Dr. John Rioux**, Associate Professor of Medicine at the University of Montreal, Montreal, Quebec; holder of the Canada Research Chair in Genetics and Genomic Medicine of Inflammation

It's well-understood that genes govern biological processes, which in turn contributes to the disease state. In the past five years there has been huge progress in understanding the genetics of common diseases, including autoimmune diseases.

For example, we now have the ability to track 1,500 single nucleotide polymorphisms or SNPs – DNA sequence variations that occur when a single nucleotide in the genome sequence is altered. SNPs do not cause disease, but they can help determine the likelihood that someone will develop a particular disease.

Although more than 99 per cent of human DNA sequences are the same across the population, variations in DNA sequence can have a major impact on how humans respond to disease; to environmental insults such as bacteria, viruses, toxins, and chemicals; and to drugs and other therapies. This makes SNPs of great value for biomedical research and for developing pharmaceutical products or medical diagnostics.

It is likely that SARD are complex trait disorders. Unlike cystic fibrosis or Huntington's disease, for example, they are not related to a single genetic abnormality.

Armed with powerful new tools and technologies, geneticists are working to track down the causes and processes involved in SARD. However, most genetic risk factors for common diseases have little diagnostic value. Their real value is in helping scientists understand mechanisms for disease. In some cases, this may translate into useful information about prognosis and clinical management.

Some disease genes and alleles are shared by multiple autoimmune and other chronic inflammatory diseases. (An "allele" is an alternative form of a gene – one member of a pair – that is located at a specific position on a specific chromosome.) For example, PTPN22, a gene that encodes the intracellular protein tyrosine phosphatase nonreceptor, has recently been linked with Type 1 diabetes. There are also convincing associations between this gene and SLE, and also between PTPN22 and both Graves' disease and Hashimoto thyroiditis.

In the search for greater understanding of SARD, geneticists are trying so-called "targeted approaches" based on known causal alleles. They are also being guided by current knowledge of pathophysiology, public genome data, and experimental data from repository subjects (for example, microarray biopsy data). Genetic discoveries could help identify potential drug targets and also predict how well certain patients with autoimmune rheumatic disease will respond to treatment.

## Environmental Factors and Systemic Autoimmune-Related Diseases

**Dr. Glinda Cooper**, Senior Investigator in the National Institute of Environmental Health Sciences at the U.S. National Institutes of Health, Triangle Park, North Carolina; Principal Investigator of the Carolina Lupus Study

Genetic susceptibility is an important determinant of autoimmune rheumatic disease, but it's not the only determinant. Studies of disease concordance in identical twins show that the contribution of genetics varies: for example, if an identical twin develops systemic lupus erythematosus (SLE), there is a 25 to 35 per cent chance that his or her twin will also develop SLE (vs. five percent for a non-identical sibling).

While genetic factors likely play an important role in systemic autoimmune-related diseases, there is growing evidence that environmental agents may also influence the development or progression of some of these diseases. Some environmental exposures seem to have fairly specific effects (i.e., they are associated with only one or two diseases). Others appear to have broader effects, influencing the development of several different diseases. For example:

**Scleroderma and exposure to solvents** In the 1970s, researchers linked a scleroderma-like disease with exposure to vinyl chloride. Since then, more than ten epidemiologic studies have been conducted on this topic. They generally show that people in occupations which exposed them to solvents were two to three times more likely to develop scleroderma than those who were not exposed. Other studies have linked solvents to a higher risk of systemic vasculitis and rheumatoid arthritis, but there is very little data from studies in humans suggesting a link between solvent exposure and SLE. Several experimental studies examining the effect of the solvent trichloroethylene in lupus-prone mice have been reported, and these studies are helping to elucidate the mechanisms through which solvents may affect autoimmune disease development, expression and progression.

**SLE, scleroderma and systemic vasculitis and exposure to silica** Studies have shown fairly strong associations between exposure to silica dust and three types of systemic autoimmune-related diseases: SLE, scleroderma and systemic vasculitis (as well as rheumatoid arthritis). Silica dust, which comes from quartz, is encountered in many types of construction work, stonework, some kinds of mining, and work that involves abrasive grinding. Respirable silica dust is easily trapped in the lungs where it may trigger an immune response. There is evidence that exposure to silica dust enhances immune response by stimulating pro-inflammatory cytokines (IL1, TNF $\alpha$ ) and also increases apoptosis of cells.

Dr. Cooper was the principal investigator of the Carolina Lupus Study, an epidemiologic study of risk factors for SLE. The study included 265 cases and 355 controls living in 60 counties in North Carolina and South Carolina. Researchers collected information using structured in-person interviews that focused on reproductive and occupational histories. Blood samples were obtained from 92 per cent of the cases and from 85 per cent of the controls.

The results for the analysis of occupational exposure to silica dust in relation to risk for SLE were "striking," Dr. Cooper said. There was a dose-response across levels of exposure, with an approximate two-fold increased risk in the medium exposure category and four-fold increased risk in the high exposure category. As expected, the prevalence of high exposure was lower among women compared with men, but the associations were seen in both groups (Parks et al.,

*Arthritis Rheum*, 2002). Results for other occupational exposures have recently been published (Cooper et al., *J Rheum*, 2004).

**Exposure to farm work and systemic vasculitis** Recent studies have found fairly strong associations between exposure to farm work and the later development of systemic vasculitis. It is unclear what component or components of farm work may be implicated, since farm workers are routinely exposed to solvents, pesticides, animals, dust (including silica dust) and ultraviolet (UV) radiation. (High UV exposure has been associated with lupus flares and with the dermal features seen in lupus and in dermatomyositis.)

When it comes to studying potential environmental triggers for systemic autoimmune-related diseases, many questions remain to be answered. These include characterizing and quantifying the effects of different timing and intensity of exposures to suspected contaminants. There may also be some genetic susceptibility to autoimmune related effects.

This is an area where more research is needed. In general, we can say that the effect of some environmental exposures is consistent across many systemic autoimmune rheumatic diseases. But the effect of other exposures is limited to only some diseases. Also, relevant environmental exposures are not limited to those occurring near disease onset. Studies of the pre-clinical state (development, persistence and progression of autoreactive cells) may be particularly useful.

## **Scientific Presentations**

### **Sunday, December 4, 2005**

## **Lessons Learned From Past Research on SARD**

**Dr. Matthew H. Liang**, *Professor of Medicine, Harvard Medical School, Professor of Health Policy and Management, Harvard School of Public Health in Boston, Massachusetts; Chief of Rheumatology at the VA Boston Healthcare System*

Because SARD are so complex – in their phenotypic expression, in their progression and in their potential etiologies – researchers will have to be creative to study them. Experience shows that cross-disease, cross-discipline research requires a steady commitment of time and funding. A number of investigator-initiated, multi-site clinical studies have already been done to learn more about these diseases, and many others are now underway. They highlight the special challenges of doing SARD research:

**Recruitment** SARD are relatively rare diseases (i.e. compared to many cancers or diseases like diabetes and osteoporosis), and this limits the number of available study participants. Multi-site studies are often needed, and these are expensive to mount and complete. Experience shows that achieving target sample sizes is a challenge; only ten per cent of “eligibles” are actually enrolled. Each exclusion criterion disqualifies 15 per cent of potential subjects.

**Hidden costs** Researchers often underestimate the real resources which are necessary to get definitive answers to study questions – for example, transportation costs for bringing subjects in to the study centre; the costs of ensuring quality control in data collection; the development of

sites and/or monitoring of participants. They may not realize just how much “ramp-up” time is necessary to conduct high-quality, multi-site, multi-disciplinary research.

**Scientific leadership** This is vital when setting up multi-site, multi-disciplinary ventures like CaNIOS. (CaNIOS is a group of Canadian investigators which formed a decade ago to improve the outcomes of lupus patients across the country through collaborative research.) While scientists can be trained, leaders need to be grown or recognized.

What is the phenotype of a scientific leader? This person must create a safe haven for vetting ideas and making judgments, must nurture and protect team members and must constantly be recruiting. Such leaders state the problem, not the solution. For the SARD research agenda to move forward, we need “visionary scientists who are interested in doing what no one has done, and in seeing what no one has seen.”

## Experience From Germany

*Dr. Falk Hiepe, Professor of Rheumatology and Consultant at the Department of Medicine (Rheumatology and Clinical Immunology), Charité University Hospital, Berlin.*

Because of the challenges involved in doing SARD research, there is a need for innovative models and partnerships. One such model exists in Germany. It's called the Network for Innovative Rheumatology Diagnostics and Therapeutics and is sponsored by the German Ministry of Economics and Labor. The aim of the Network is to connect small and medium-sized enterprises with research centres to promote collaboration in the field of rheumatology.

By implementing the Netzwerk-Management-Ost (NEMO) project in 2002, the German government wanted to create new impetus for innovative networks. The NEMO program is intended to create a network that opens new cost advantages and market opportunities mainly for small businesses. This will enable them to perform complex and/or interdisciplinary research and to rapidly transform research results into marketable products, procedures and services. Eligible networks may receive subsidies to cover part of their network planning and management costs.

A number of projects have been or are in the process of being implemented. They include: the development of a peptide-based ELISA test system for the diagnosis of rheumatic diseases; studies on the development of a rapid test for rheumatic disorders; and research on the use of targeted cellular therapies in systemic lupus erythematosus.

The ultimate goal is to develop commercially feasible diagnostic and therapeutic innovations for rheumatic diseases that become available to patients more quickly, thanks to integrated cooperation between researchers and industry.

## Experience From the U.S.

**Dr. Maureen Mayes**, *Professor of Medicine at the University of Texas Medical School in Houston, Texas; Director of the Scleroderma Clinic and Principal Investigator of the Scleroderma Family Registry and DNA Repository*

U.S. researchers are currently probing the role of genetic factors in scleroderma. They want to learn more about what makes people susceptible to this potentially serious disease and why it is more severe in some patients than in others.

Many clinical trials have been done to see whether certain drugs or other biological agents might block the development of fibrosis, which is a key feature of scleroderma. Agents which have so far proved ineffective include: d-penicillamine, methotrexate, interferon alpha, collagen and recombinant human relaxin.

One substance, cyclophosphamide (CYC) has shown promise in preventing lung fibrosis. The same drug has shown benefits in slowing skin thickening, improving lung function and improving quality of life in a group of patients with scleroderma.

The Scleroderma Lung Study was a randomized, double-blind, concurrent study of cyclophosphamide at up to 2mg/kg for 12 months or placebo for 12 months, followed by 12 months of observation. The adjusted mean difference between CYC and placebo was 2.32 (95% C.I.: -0.04 to 4.70) favouring CYC ( $p = 0.053$ ). There were significant differences in mean adjusted skin scores in favour of CYC.

The trial presented many challenges. Low disease prevalence and incidence necessitated a multi-centre clinical trial. Enrollment was usually targeted to subsets of patients which further decreased the pool of eligible subjects.

Another randomized, multi-centre U.S. trial (announcement of a possible Canadian site is pending) will look at 12 months of IV CYC versus high-dose immunoablative chemotherapy followed by stem cell rescue for early, diffuse scleroderma with significant internal organ involvement. Known as the SCOT (Scleroderma Cyclophosphamide or Transplant) trial, this large study is expected to answer key questions about the future of immunosuppression in treating scleroderma.

## An Introduction to Theranostics

**Dr. Marvin Fritzler**, *Professor of Medicine, Departments of Medicine and Biochemistry and Molecular Biology, the University of Calgary, Calgary, Alberta*

A new field is emerging that combines methods for diagnosing SARD with the ability to treat these diseases. It's called "theranostics" and includes the use and application of sophisticated tests and technologies. So what will the field of theranostics look like ten years from now?

Systemic autoimmune diseases are characterized by extensive alterations in immune system function, with cytokines and autoantibodies contributing to impaired immunoregulation and tissue damage. In the near future, scientists will have a clearer understanding of the expression

and function of cytokines and adipokines (hormones secreted by adipose tissue), which may play a role in autoimmune dysregulation.

The field of metabolomics will be yielding new information about SARD. Metabolomics is the systematic study of the unique chemical fingerprints that specific cellular processes leave behind – specifically, it involves exploring small-molecule metabolite profiles.

There will also be a clearer understanding of the role played by the innate immune system – particularly how PAMPs (pathogen-associated molecular patterns) and PRRPs (pattern recognition receptor profiles) protect – or fail to protect – against autoimmune disease.

## New Approaches in Diagnostics

*Dr. Paul Utz, Associate Professor of Medicine in Rheumatology and Immunology at Stanford University School of Medicine in Stanford, California.*

Scientists who seek new and better ways to diagnose SARD will employ robotic cell and tissue arrayers to test hundreds of blood samples at once, using manufactured antigens that will bind with abnormal antibodies. Such arrayers could be used to help guide development of a potential treatment for a particular autoimmune disease and also to monitor treatment and disease progression.

Other diagnostic technologies which may be in broader use over the next decade – both for research and to track treatment and disease progression – will include: addressable laser bead assays (ALBA); antigen/analyte arrays on planar surfaces; microfluidics (lab on a chip); Matrix-Associated Laser Desorption Ionization (MALDI) Time of Flight (TOF) mass spectrometry; and nanotechnology. (Nanotechnology is the understanding and control of incredibly tiny bits of matter. A nanometer is one-billionth of a meter; a sheet of paper is about 100,000 nanometers thick.)

## Elements of Designer Therapeutics

*Dr. Joachim Kalden, Professor of Internal Medicine, Clinical Immunology and Rheumatology, University of Erlangen-Nuremberg, Bavaria, Germany.*

As a group of diseases, SARD presents a challenge to researchers looking for clues about etiology, progression and treatment. Even today, no effective treatment principles exist for Sjögren's syndrome, SLE, polymyositis and Wegener's granulomatosis (a type of vasculitis in which blood vessels become inflamed, damaging the respiratory system and kidneys).

Before progress can be made towards developing new treatments, researchers must learn more about causes, genetic predispositions, co-factors (other illnesses or common events),

Researchers must consider the heterogeneity of any given rheumatic disease entity. There are considerable variations in clinical appearance, clinical course and outcomes, serological parameters and responses to existing medications.

Certain prerequisites exist before researchers can make progress towards novel treatment principles for autoimmune diseases. There is a real need for basic information about genetic predisposition and pharmacogenetics; about co-factors such as infectious agents; about the implications of autoantigens; and about potential mechanisms for both tissue destruction and repair. More information is also needed about how each disease progresses and why some patients go into remission.

Novel treatment targets might include: susceptibility or protective genes; cellular and/or humoral components of the immune system involved in disease-specific tissue destruction; and molecules responsible for tissue repair mechanisms

For example, there has been interest in the clinical efficacy of tumour necrosis factor-alpha (TNF- $\alpha$ ). It is known that over-expression of TNF- $\alpha$  acts as a driver for inflammation; this suggests that TNF- $\alpha$  inhibitors may be helpful in treating autoimmune rheumatic diseases. These agents have proven effective (especially when added to other disease-modifying anti-rheumatic drugs) and relatively safe. However, the majority of patients only respond to a limited extent, and only two-thirds (60 to 65 percent) respond positively to currently available TNF- $\alpha$  antagonists. Indeed, there may be some contraindications for using a TNF- $\alpha$  antagonist.

Scientists are already exploring components of the human immune system which may lead to new treatments or even to prevention of SARD. They include proteins called "Toll-like receptors" or TLR, heat shock proteins, chemokines and chemokine receptors and galectins – a family of proteins that have been strongly implicated in inflammation and cancer.

Some agents have proven systemically effective (for example, Interferon- $\alpha$  for lupus), while others have been locally effective (for example, Interferon- $\gamma$  and TNF- $\alpha$  for SLE nephritis).

Promising future targets for immune intervention include: T-cells and B-cells; adhesion molecules (ICAM-1, VCAM-1 and E-selectin); the TNF family molecule RANKL (receptor activator of NF- $\kappa$ B ligand); and c-Jun NH2-terminal kinases (JNKs) which are involved in regulating the expression of cytokine genes.

Researchers are also studying the usefulness of autologous stem cell transplantation to remodel the immune systems of patients severely affected by SARD. They are also exploring the benefits of combination therapy (i.e. combining biologicals with other biologicals or with immunosuppressive agents); looking at the potential for gene therapy; and testing out various vaccination and anti-sense strategies. ("Antisense" drugs are based on the fact that antisense RNA hybridizes with and inactivates "messenger RNA" (mRNA). These drugs stop a particular gene from producing the protein for which it holds the recipe. Antisense drugs are being developed to treat lung cancer, diabetes and diseases like SARD which have a major inflammatory component.)

Also on the horizon for therapeutic targeting is a potent pro-inflammatory cytokine called the high mobility group box 1 protein (HMGB1) which is released by necrotic cells and triggers inflammation.

## **Consensus Conference on Systemic Autoimmune Rheumatic Diseases (SARD): A Research Forum on Lupus, Scleroderma, Sjögren's Syndrome, Autoimmune Myositis and Vasculitis**

### **Consensus Report and Recommendations**

Following the Consensus Conference, a Working Group met to consider all the small group reports and recommendations about Systemic Autoimmune Rheumatic Diseases identified by conference participants.

The members of this Working Group are: Dr. Paul Fortin, Dr. Marvin Fritzler, Dr. Aileen Davis, Dr. John Hanly, Dr. Christine Peschken, Dr. Robin Poole, Dr. Murray Baron, Dr. Rae Yeung and Louise Bergeron (consumer representative).

The Working Group discussed key issues which must be addressed in developing an Action Plan for SARD:

#### **There are unique, unmet needs associated with SARD.**

As a group of diseases, SARD does not have a home. There is no infrastructure for integrated SARD research, patient care and knowledge translation and exchange. The following five unmet needs summarize the existing situation in Canada and underscore the need for a coordinated and focused action plan:

- Scientists don't know when, how or why these diseases start and progress.
- Access to appropriate care is sub-optimal.
- There is a general lack of awareness about SARD, including the consequences of these diseases.
- There are few effective treatments and no cures.
- The actual burden of SARD in Canada is unknown.

#### **Barriers exist which prevent us from meeting these needs.**

The following barriers must be considered before these unmet needs can be positively addressed:

- Modern research is complex, and it is difficult to explain the challenges given limited public awareness about SARD.
- We lack the necessary "critical mass" of researchers and support personnel to launch a coordinated research plan.
- The current funding environment is also difficult and complex.
- Networks for communication and collaboration around SARD research are limited or unexploited.

**To make progress, we must assert and follow Strategic Directions.**

“Strategic Directions” refers to a comprehensive framework that will guide all existing and emerging activities within the SARD research and care community. The 2005 SARD Consensus Conference identified three key strategic directions for SARD research in Canada.

- We will move towards a recognized Canadian presence in the field of SARD research.
- We will work towards building dynamic working partnerships.
- We will aim to develop an integrated, Canada-wide research agenda for SARD.

**We have developed and will continue to refine a SARD Action Plan.**

The Action Plan spells out immediate steps recommended by the Working Group to focus existing and new activities over the next six to nine months.

Details of the Action Plan for SARD are NOT included in these Scientific Proceedings, but can be viewed on the SARD website ([www.sardcommunity.org](http://www.sardcommunity.org)). The Action Plan is a dynamic document which will be updated on a regular basis.

The anticipated benefits of the SARD Action Plan fall into three areas:

**Treatment** Treating patients with SARD is important. Steps must be taken to streamline the current system so patients are referred to the appropriate specialists for optimal treatment . When this is achieved, the diagnosis will be made much earlier and the appropriate specialist can institute the best possible, evidence-based treatment in a timely manner. This will decrease and limit disease burden.

**Research** The first line of defence in medicine is prevention. To accomplish this with respect to SARD, we must obtain a better understanding of how and why the diseases begin in the first place. If prevention is not possible, then the next most important step is early diagnosis. Research is needed to provide more sensitive and specific tools for diagnosis and to develop new therapies tailored to the individual patient.

**Collaboration** Efforts must be made to coordinate the activities of basic and clinical scientists, other academics, health care and support organizations and patients. This will create the best possible environment to ensure that meaningful new information about SARD is translated into practical approaches to diagnosis and treatment.

*See Appendix V for details on the Action Planning Framework and a history of the SARD Action Planning Document.*

**Consensus Conference on Systemic Autoimmune Rheumatic Diseases (SARD):  
A Research Forum on Lupus, Scleroderma, Sjögrens Syndrome,  
Autoimmune Myositis and Vasculitis**

**Appendix I: Conference Agenda**

**Consumer Orientation Day** (Co-Chairs, Cheryl Magnusson, Pamela Bowes)  
**Friday, December 2, 2005**

**9:00 – 10:00 Breakfast and Informal “Meet and Greet”**

<b>10:00 – 10:30</b>	<b>Welcome/Bienvenue</b> Review Purpose of the conference Review Purpose of the Consumer Day Review how the Conference will function	Cheryl Magnusson Dr. Paul Fortin Cheryl Magnusson Dr. Paul Fortin
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<b>10:30 – 12:00</b>	<b>How is Medical Research Funded in Canada? How Does it Work?</b> Role of CIHR Institutes Role of CAN (Canadian Arthritis Network)	Dr. Aileen Davis Dr. Jane Aubin
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*Refreshment Break*

Role of health charities	Bonnie Thorn
Role of the pharmaceutical industry	Chris Nelson

**12:00 – 1:30** *Lunch*

<b>1:30 – 2:30</b>	<b>Consumers as Patient Advocates</b> What are some of the opportunities? What is involved? What has been the experience of some other groups? What are some of the issues facing patients with Systemic Autoimmune Rheumatic Diseases?	Catherine Hofstetter/Denis Morrice
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*Refreshment Break*

<b>2:45 – 3:30</b>	<b>Overview of Scientific Program for Dec. 3 &amp; 4, 2005</b> What are the research areas that will be discussed? Why are they important to people living with Systemic Autoimmune Rheumatic Diseases?	Dr. Paul Fortin
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<b>3:30 – 4:00</b>	<b>Meeting Summary and Termination</b>	Cheryl Magnusson/Pamela Bowes
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## Scientific Presentations (Day One)

Saturday, December 3

Time	Topic	Speakers
8:00	<b>Welcome/Bienvenue</b>	<b>Marvin Fritzier/Paul Fortin</b>
	<ul style="list-style-type: none"> <li>• Overview/Conference Objectives</li> </ul>	
	<b>Setting the Stage – Opening Statements</b>	
	<ul style="list-style-type: none"> <li>• Where we Are, Where we're going, What are the Needs</li> </ul>	<b>Bhagirath Singh</b>
	<b>Process – How the Conference will Function</b>	<b>Jerry Mings (meeting facilitator)</b>
	<b>Moderator: Ann Clarke</b>	
	<b>Burden of SARD - Frequency, Outcomes</b>	
8:45	1.1 Facts and Numbers – The epidemiology of SARD	<b>Sherine Gabriel Christine Peschken</b>
	1.2 SARD in Minority Groups (Aboriginals)	
10:00-10:15	Questions	
10:15-10:30 <i>Refreshments</i>		
	<b>Moderator: Andrew Leask</b>	
	<b>2.0 Pathophysiology: What is different and what is similar amongst SARD</b>	
10:30	2.1 B-cells and T-cells – What have we learned about the pathophysiology of SARD from studies of human and animal models?	<b>Mary Crow</b>
	2.2 Genetics and SARD	
	2.3 Learning from the field – Environmental factors and SARD	
12:00-12:15	Questions	<b>John Rioux Glinda Cooper</b>
12:15–1:15 <i>Lunch Break</i>		

**Moderator: Claire Bombardier**

**3.0 SARD Research in Canada and Challenges in Coordinating Multi-Centre Research**

**2:15**      **3.1** Lessons Learned from past research on SARD      **Matthew Liang**  
**3.2** NRC in Autoimmune Disorders - Experience from Germany      **Falk Hiepe**  
**3.3** Experience from USA      **Maureen Mayes**

**3:15-3:30**      Questions

**3:30 – 3:45**      *Refreshments*

**3:45-4:45**      *Breakout Session 2: Priorities for SARD research in Canada*

**1:15-2:15**      *Breakout Session 1: Identify the most important research topics to better understand the disease process and impact of SARD in Canada*

**4:45-5:00**      **Wrap-up**      **Jerry Mings**

**5:30–7:00**      **Cocktail Reception**

**7:00-9:00**      **Dinner and Guest Speaker**      **The Honourable, Dr. Carolyn Bennett, PC, MP,  
Minister of State (Public Health)**

## Scientific Presentations (Day Two)

Sunday, December 4

Time	Topic	
7:30	<i>Continental Breakfast</i>	
9:00	<b>Synopsis of Day One Work Group Deliberations</b>	<b>Jerry Mings</b>
	<b>Moderator: Marvin Fritzler</b>	
	<b>4.0 Theranostics - The merging of Therapeutics and Diagnostics</b>	
9:15	4.1 Introduction on Theranostics	<b>Marvin Fritzler</b>
	4.2 New approaches in diagnostics: Array Technologies	<b>Paul Utz</b>
	4.3 Elements of designer therapeutics	<b>Joachim Kalden</b>
10:30-10:45	Questions	
10:45-11:45	<b><i>Breakout session 3: Addressing the challenges of conducting multi-national multi-centre SARD research.</i></b>	
11:45-1:00	<b><i>Wrap-up</i></b>	<b>Jerry Mings</b>
1:00	<i>Lunch</i>	

**Consensus Conference on Systemic Autoimmune Rheumatic Diseases (SARD):  
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**Appendix II: List of Scientific Presenters (in alphabetical order)**

***Glinda Cooper, Ph.D.***

Dr. Glinda Cooper is a Senior Investigator in the Epidemiology Branch of the National Institute of Environmental Health Sciences, one of the institutes of the National Institutes of Health (United States). She received a doctoral degree from the Department of Epidemiology of the University of North Carolina at Chapel Hill in 1993, and also has a master's degree in Health Policy and Management from Harvard School of Public Health.

Dr. Cooper's research interests concerns the genetic, hormonal, and environmental influences on diseases that disproportionately affect women. A major component of this work has been on autoimmune diseases, particularly the prototypical disease, systemic lupus erythematosus. Dr. Cooper is the Principal Investigator of the Carolina Lupus Study, the first population-based case-control study of hormonal and occupational risk factors for lupus conducted in the United States. This study was designed to explore environmental influences, and the interaction between specific environmental exposures and susceptibility genes, to the etiology of lupus.

Dr. Cooper is now expanding her research to include other autoimmune diseases, such as systemic vasculitis, systemic sclerosis and rheumatoid arthritis, and to focus on the pre-clinical phase of disease to further elucidate the role of environmental exposures in the development of autoreactive cells and the progression to clinically overt autoimmune disease.

***Mary K. Crow, M.D.***

Dr. Mary K. Crow holds the Benjamin M. Rosen Chair in Immunology Research and is Senior Scientist and Associate Chief for Rheumatology Research at the Hospital for Special Surgery in New York. She is Co-Director of the Mary Kirkland Center for Lupus Research and Director of the Autoimmunity and Inflammation Program at Hospital for Special Surgery. Dr. Crow is also Professor of Medicine

***Marvin J. Fritzler, PhD MD***

Dr. Marvin Fritzler was born and educated in Alberta, receiving his B.Sc. from the University of Alberta in 1968, his PhD from the University of Calgary in 1971 and a MD from the University of Calgary in 1971. Following post-graduate training at the Scripps Research Institute in La Jolla, California and the University Medical Center in Denver, Colorado, Dr. Fritzler joined the Faculty of Medicine at the University of Calgary in 1978. From 1996 to 2001, Dr. Fritzler was Associate Dean Research of the Faculty of Medicine at the University of Calgary. In 2001, he was appointed as the Arthritis Society Chair.

Dr. Fritzler's research interests are the development of new diagnostic technologies for autoimmune diseases. He has published more than 220 papers and book chapters and has been a contributor to many national and international organizations; he has been President of the Western Section of the American Rheumatism Association and the Canadian Society of Clinical Investigation.

He served on the Scientific Advisory Board of the EPA Center for Environmental Health Sciences at the University of Montana. He is an active member and past chair of the Serology Committee of the International Union of Immunology Specialists and World Health Organization. He is currently Chairman of the Government of Alberta's Board of Directors of the Alberta Science and Research Authority (ASRA).

### ***Sherine E. Gabriel, MD, MSc***

Dr. Sherine Gabriel received a Doctor of Medicine degree, with distinction, from the University of Saskatchewan, Canada in 1982. Following a one-year rotating internship at the University of Manitoba Teaching Hospitals, she completed Internal Medicine Residency and Rheumatology fellowship at the Mayo Graduate School of Medicine in Rochester, Minnesota. Dr. Gabriel then pursued advanced training in research methods at McMaster University in Canada where she was awarded a Master of Science in Clinical Epidemiology in 1991. She is certified by the American Board of Internal Medicine in both Internal Medicine and Rheumatology and holds dual appointments as Mayo Clinic Consultant in the departments of Internal Medicine/Rheumatology and Health Sciences Research/Epidemiology. She is Professor of Epidemiology and of Medicine at the Mayo Clinic College of Medicine. Dr. Gabriel is also the William J. and Charles H. endowed professor.

Dr. Gabriel is Chair of the Department of Health Sciences Research (HSR), the largest research department at Mayo Clinic. HSR staff includes 405 research professionals in four different divisions: Biostatistics, Epidemiology, Health Care Policy & Research, and Biomedical Informatics. The mission of the department is to improve the care of patients and reduce the burden of human illness through investigator initiated research and research collaborations led by department members, and through the development of research infrastructure in support of the larger scientific community at Mayo.

Dr. Gabriel has successfully integrated her knowledge of clinical rheumatology with her training in epidemiology and health services research to develop a research program that has made important contributions to our understanding of the risks, determinants, and outcomes of the rheumatic diseases. Her research falls under three main methodological categories: population epidemiology, clinical epidemiology, and health services/outcomes research. A few highlights include her many publications on the risks, costs, and cost-effectiveness of non-steroidal anti-inflammatory drugs (NSAIDs), her well known epidemiologic studies examining the risks of connective tissue diseases among women with breast implants, her population-based studies characterizing the epidemiology of nearly all the major rheumatic diseases (e.g. RA, JRA, SLE, GCA, PMR, psoriatic arthritis, localized scleroderma), and her studies defining the economic impact of RA. Her current research is focused on elucidating the risks and determinants of heart disease among persons with rheumatoid arthritis. Altogether, her research has resulted in 299 publications with over 2400 citations.

Dr. Gabriel's research has been widely recognized, nationally and internationally. This is evidenced by her role on several editorial boards, her service on numerous NIH and AHCPR

study sections; and her leadership roles in both the Arthritis Foundation and the American College of Rheumatology. She recently completed a four-year term on the Board of Directors of the American College of Rheumatology (ACR), and currently chairs the ACR Quality Measures Committee.

Dr. Gabriel's commitment to clinical research also extends to clinical research education. With funding from the NIH she developed the Mayo Clinical Research Training and Career Development Programs. These programs offer a structured clinical research curriculum combined with a mentored clinical research practicum leading to either a Master's degree or a Certificate in Clinical Research. The programs have been a resounding success, received enthusiastically by both faculty and participants. In fact, the Masters degree in Clinical Research has rapidly become the largest and most highly sought after program at Mayo Graduate School.

### ***Theodor Falk Hiepe***

Dr. Falk Hiepe is a professor of Rheumatology and Consultant at the Department of Medicine (Rheumatology and Clinical Immunology), Charité University Hospital in Berlin, Germany. He did his medical training at Humboldt-University at Berlin where he also completed his PhD. He has held the position of Guest Professor at the Second Department of Medicine of the Teikyo University and at the Department of Medicine and Physical Therapy of the University of Tokyo (Japan). In 1995 he was at the Scripps Research Institute in La Jolla, California. He is appointed as a Professor of Medicine (Rheumatology and Clinical Immunology) at the Humboldt-University of Berlin; and as group leader (group autoimmunity) at the German Rheumatism Research Center in Berlin.

Dr. Hiepe is a member of the German Society of Rheumatology, the American College of Rheumatology, a member of the SFB 421 (supported by the Deutsche Forschungsgemeinschaft); a member of the SFB (supported by the Deutsche Forschungsgemeinschaft); a member of the Japan Rheumatism Association. He also sits on the Drug Commission of the German Medical Association and is on the International Advisory Board of Modern Rheumatology.

Dr. Hiepe editorship includes the textbook "Interdisziplinäre klinische Rheumatologie" (Eds. Zeidler, Zacher, Hiepe), Springer Heidelberg Berlin NewYork, 2001; and Autoantibodies in systemic autoimmune diseases (Eds. Conrad, Schöfler, Hiepe

He is the recipient of the Humboldt-Award of the Humboldt-University of Berlin for the best Diploma, Research Award of the Charité, and Award of the Donation Wolfgang Schultze.

His primary research interests include, systemic autoimmune disease; diagnostic and pathogenic relevance of autoantibodies; role of long-lived plasma cells in autoimmunity; and innovative therapeutic approaches in autoimmune disease.

### ***Joachim R. Kalden, MD***

Dr. Joachim Kalden is a professor in the Department of Internal Medicine III and Institute for Clinical Immunology and Rheumatology, University Erlangen-Nuremberg. He is a graduate of the University of Tübingen.

Since 1982 Dr. Kalden has been a member and chairperson of numerous national and international scientific committees related to clinical immunology and rheumatology. Dr. Kalden is the Past-President of EULAR and is currently the Chairman of the Curatorship of the Carol-Nachman Award, one of the most prestigious rheumatology awards in the world. Dr. Kalden is a member of many national and international scientific societies. Likewise he is a member or has served as a member of the advisory or editorial boards of national and international journals. His review and advisory activities comprise different national and international foundations. His bibliography comprises more than 500 original papers published in international journals and an equal number of reviews and textbook chapters.

Dr. Kalden has been involved in the organization of quite a number of national and international scientific meetings. He has received many awards, most recently the honorary doctorate of the Medical Faculty Lund, Sweden 2005 and honorary membership of national and international societies of rheumatology and immunology.

### ***Matthew H. Liang, MD, MPH***

Dr. Matthew Liang is a Professor of Health Policy and Management at Harvard School of Public Health and is currently based at the Brigham and Women's Hospital and the Massachusetts Veteran's Epidemiology Research and Information Center (MAVERIC). He is a graduate of Johns Hopkins University in philosophy and chemistry, Harvard Medical School, and the Harvard School of Public Health (HSPH) in tropical public health and epidemiology.

He founded and directed the Robert B. Brigham Arthritis and Musculoskeletal Diseases Clinical Research Center at the Brigham and Women's Hospital between 1977-2002 and is currently its Director of Special Projects. He is Medical Director of Rehabilitation Services at Brigham and Women's Hospital. Dr. Liang is a founding faculty member of the Clinical Effectiveness Program at HSPH and is a member of the BWH Research Institute's Clinical Research Committee.

Dr. Liang also directs the Center for Advanced Methodological Support for Innovative SLE Trials (ASSIST), and is the Chief of the Section of Rheumatology at the VA Boston Healthcare System, and a Study Director in the VA Cooperative Studies Program (CSP). The CSP has conducted over 550 multi-centre clinical trials since its inception. Dr. Liang has served on the Advisory Council of the National Institute of Arthritis, Musculoskeletal and Skin Diseases, and is currently on the Boards of the Alliance for Lupus Research, the Lupus Clinical Trials Consortium, and Rheuminations, Inc. He serves on the editorial boards of *Arthritis and Rheumatism*, *Lupus*, *SPINE*, *The American Journal of Medicine*, *Patient Care*, and *Current Rheumatology Reviews*. He is an active primary care physician and rheumatologist and was named one of the Best Doctors in America.

He is a recipient of the Lawrence Poole Prize in Rehabilitation from the University of Edinburgh, the Lee C. Howley Sr. Prize for Research in Arthritis, the Kirkland Scholar Award and the American College of Rheumatology Award of Distinction for Clinical Research. He is a consultant to the Food and Drug Administration, the Shriners Hospital - Boston, Hong Kong Research Council, the Arthritis Research Centre of Canada, and the Office of the Clinical director of the Intramural Research Program of the National Institute of Arthritis and Musculoskeletal and Skin Diseases.

His current research interests include basic methodologic work in clinimetrics, clinical trials methodology in systemic lupus erythematosus, the epidemiology of rheumatic disease and disability, prevention of Lyme disease, outcomes research, the identification of modifiable risk factors in high risk and disadvantaged populations, clinical decision making, and prevention of osteoarthritis.

### ***Maureen D. Mayes, MD, MPH***

Dr. Maureen D. Mayes is Professor of Medicine at the University of Texas Medical School in Houston where she is the Director of the Scleroderma Clinic. She is the author of more than 50 articles relating to scleroderma, its complications and its treatments. In addition, she is the author of *The Scleroderma Book: A Guide to Patients and their Families* published by Oxford University Press.

Dr. Mayes graduated from Eastern Virginia Medical School in Norfolk, and did her postgraduate training in Internal Medicine and Rheumatology at the Cleveland Clinic in Cleveland, Ohio.

Dr. Mayes obtained her Masters of Public Health at the University of Michigan where she studied the epidemiology of scleroderma, particularly the role of environmental exposures in the development of this disease. As Principal Investigator of the Scleroderma Family Registry and DNA Repository, she is currently studying the role of genetic factors in scleroderma susceptibility and disease severity. She has participated in numerous multi-centre trials on scleroderma and its complications.

### ***Christine Peschken, MD***

Dr. Christine Peschken graduated from University of Saskatchewan School of Medicine in 1989, specializing in Internal Medicine and Rheumatology (1995) at the University of Manitoba. She did an Arthritis Society Research Fellowship under Dr. John Esdaile's supervision, 1996-1998, including a Master's degree in Epidemiology and Biostatistics from McGill University. Dr. Peschken is an assistant professor at the University of Manitoba and Rheumatologist/researcher at the Health Sciences Centre and St. Boniface General Hospital. Her current research interests include systemic lupus erythematosus and rheumatic diseases in Aboriginal Canadians.

### ***John Rioux, PhD***

Dr. John Rioux is currently an Associate Professor of Medicine at the University of Montreal and holds the Canada Research Chair in Genetics and Genomic Medicine of Inflammation. In addition, Dr. Rioux is an Associate Member the Broad Institute of MIT and Harvard.

During his PhD., Dr. Rioux performed molecular studies designed to examine the anti-viral immune response in the chronic inflammatory diseases rheumatoid arthritis and systemic lupus erythematosus (SLE). Dr. Rioux directed multiple studies of the genetic susceptibility to inflammatory diseases at the Broad Institute between 1995-2005. He continues to oversee the projects ongoing at the Broad Institute and has started a new Laboratory of Genetics and Genomic Medicine of Inflammation at the Montreal Heart Institute of the University of Montreal. Dr. Rioux has directed and/or participated in collaborative genetic studies of multiple human diseases including inflammatory bowel diseases (IBD), systemic lupus erythematosus (SLE),

multiple sclerosis (MS), rheumatoid arthritis (RA), celiac disease, asthma, and coronary artery disease. Dr. Rioux's group co-discovered the haplotype structure of the human genome and has identified numerous disease susceptibility loci. Dr. Rioux's group also reported the first SNP-based map of the patterns of genetic variation in the MHC region and is leading an international effort to generate a comprehensive haplotype map of this region. His group continues to develop and employ genetics and genomics approaches to obtain a better understanding of the molecular mechanisms that are involved in susceptibility and phenotypic expression to common inflammatory diseases.

### ***Bhagirath Singh, MD***

Dr. Bhagirath Singh is currently Scientific Director of the Institute of Infection and Immunity of the Canadian Institutes of Health Research (CIHR), a Professor in the Department of Microbiology and Immunology at the University of Western Ontario, and a Scientist at the Robarts Research Institute in London, Ontario.

After post-doctoral training at Liverpool University in England, he joined the Department of Immunology at the University of Alberta, Edmonton, Alberta in 1973 and became Professor of Immunology in 1986. From 1992-2001 he was Professor and Chair of the Department of Microbiology and Immunology at the University of Western Ontario in London, Ontario. In 2001 he was appointed the founding Scientific Director of the CIHR Institute of Infection and Immunity. He did his PhD in the chemistry of cardio-active glycosides from medicinal plants and post-doctoral work in peptide chemistry and antigen presentation to T cells using peptide epitopes.

Dr. Singh is recognized as a leader in the field of autoimmunity and the immunology of peptides. His work on the regulation of autoimmune diabetes laid the foundation of the current "hygiene hypothesis" for autoimmune diseases. He has published over 180 peer-reviewed papers. He was an Alberta Heritage Foundation for Medical Research Scholar and Scientist and has been a recipient of University of Western Ontario Faculty of Medicine Award of Excellence. He was Banting and Best Memorial Lecturer at the 17th International Diabetes Federation Congress in 2000 and Bernhard Ciner Award Lecturer at the Canadian Society for Immunology meeting in 2001. In 2004 he was elected Fellow of the Royal Society of Canada. In 2005 he was elected Fellow of the Canadian Academy of Health Sciences.

### ***Paul Utz, MD***

Dr. Paul J. (P.J.) Utz, was recently promoted to Associate Professor of Medicine in the Division of Rheumatology and Immunology at Stanford University School of Medicine. Professor Utz was born and raised in the Pocono Mountains near Scranton, Pennsylvania (PA). In 1986, he earned his Bachelor's Degree in Biology from King's College in Wilkes-Barre, PA, with minors in English and Chemistry.

While earning his MD degree in 1991 from Stanford University School of Medicine, he co-discovered the transcription factor Nuclear Factor of Activated T Cells (NFAT) with J.P. Shaw in Dr. Gerald Crabtree's laboratory. Dr. Utz completed his internal medicine residency, rheumatology fellowship, and post-doctoral training at Brigham and Women's Hospital in Boston prior to joining the Harvard Medical School Faculty in 1996. He left Dr. Paul Anderson's lab in 1999, where he studied the role of cell death and modifications of autoantigens that are targeted

in a variety of connective tissue diseases. He joined the Stanford Faculty in 1999 as an Assistant Professor.

Dr. Utz has expertise in the study of human and murine autoantibodies and autoantigens, apoptosis signaling pathways, animal models of autoimmunity, proteomics and microfluidics. Members of his laboratory are developing several cutting-edge proteomics technologies for immunological applications, including multiplex planar-based autoantigen microarrays, microfluidic capillary electrophoresis assays, and carbon-nanotube-based sensing for detection of autoantibodies in serum.

Dr. Utz is actively involved with many educational programs within the University. He is director of the CCIS Summer High School Research Program, and he provides formal lectures to undergraduate, graduate, and medical students in the School of Medicine and the School of Engineering. He also teaches medical students, residents and fellows in the clinics and on the in-patient wards, and has won teaching and mentoring awards in rheumatology (2002), immunology (2002) and medicine (2005) at Stanford.

**Consensus Conference on Systemic Autoimmune Rheumatic Diseases (SARD):  
A Research Forum on Lupus, Scleroderma, Sjögren's Syndrome,  
Autoimmune Myositis and Vasculitis**

**Appendix III List of Sponsors**

**Host Category**

The Lupus Foundation of Ontario and Lupus Canada  
The Canadian Institutes of Health Research - Institute of Musculoskeletal Health and Arthritis  
The Canadian Arthritis Network  
The Canadian Institutes of Health Research – Institute of Infection and Immunity  
The Canadian Institutes of Health Research – Institute of Gender and Health  
The Arthritis Society  
The Canadian Rheumatology Association  
The Canadian Institutes of Health Research – Institute of Aboriginal Peoples' Health  
The Scleroderma Society of Canada  
The American Autoimmune Related Diseases Association

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Autoimmune Myositis and Vasculitis**

**Appendix IV Conference Planning Committee**

<b>Paul R. Fortin, MD MPH, FRCPC</b>	<b>Conference Co-Chair</b> University Health Network Toronto Western Hospital
<b>Marvin Fritzler MD, PhD</b>	<b>Conference Co-Chair</b> Health Sciences Centre, University of Calgary, Calgary
<b>Murray Baron, MD, FRCPC</b>	McGill University Health Centre, Montreal General Hospital, Montréal
<b>Arthur Bookman, MD, FRCPC</b>	University Health Network, Toronto Western Hospital, Toronto
<b>Simon Carette, MD, FRCPC</b>	University Health Network, Toronto Western Hospital, Toronto
<b>Ricard Cervera, MD</b>	Institut d'Investigacions Biomediques August Pi i Sunyer, Spain
<b>Ann E. Clarke, MD, FRCPC</b>	McGill University Health Centre, Montreal General Hospital, Montréal
<b>John M. Esdaile, MD, MPH, FRPCP</b>	Arthritis Research Centre, Vancouver
<b>John G. Hanly, MD, MRCPI</b>	Dalhousie University, Halifax
<b>David A. Isenberg, MD</b>	Center for Rheumatology, University College London, United Kingdom
<b>Ronald M. Laxer, MD</b>	The Hospital for Sick Children, Toronto
<b>Jerry F. Payne PhD</b>	Lupus Canada Board Member
<b>Christine Peschken, MD, FRCPC</b>	University of Manitoba, Winnipeg
<b>Robin Poole, PhD</b>	Canadian Arthritis Network, Shriners Hospital for Children, Montréal
<b>John Rioux, PhD</b>	Montréal Heart Institute/Institut de Cardiologie de Montréal, Montréal
<b>Jean-Luc Senécal, MD, FRCPC</b>	Centre Hospitalier de l'Université de Montréal- Hôpital Notre- Dame, Montréal

**Consensus Conference on Systemic Autoimmune Rheumatic Diseases (SARD):  
A Research Forum on Lupus, Scleroderma, Sjögren's Syndrome,  
Autoimmune Myositis and Vasculitis**

**Appendix V List of Conference Attendees *(in alphabetical order)***

***Conference co-chairs***

**Dr. Paul Fortin**, Toronto, Ontario  
**Dr. Marvin Fritzler**, Calgary, Alberta

***Participants***

**Ms. Honey Agar**, Toronto, Ontario *(consumer)*  
**Dr. J. Antonio Avina-Zubieta**, Vancouver, British Columbia  
**Dr. Elizabeth Badley**, Toronto, Ontario  
**Dr. Murray Baron**, Montreal, Quebec  
**Ms. Louise Bergeron**, Ile Perrot, Quebec *(consumer)*  
**Dr. Sasha Bernatsky**, Montreal, Quebec  
**Dr. Raja Bobba**, Hamilton, Ontario  
**Dr. Gilles Boire**, Sherbrooke, Quebec  
**Dr. Claire Bombardier**, Toronto, Ontario  
**Dr. Arthur Bookman**, Toronto, Ontario  
**Ms. Pamela Bowes**, Toronto, Ontario *(consumer)*  
**Mr. Jody Breen**, Oshawa, Ontario *(consumer)*  
**Dr. Robin Brey**, San Antonio, Texas  
**Mr. Robert Buzza**, Montreal, Quebec *(consumer)*  
**Dr. Simon Carette**, Toronto, Ontario  
**Dr. Glinda Cooper**, North Carolina  
**Ms. Louise Crane**, Calgary, Alberta *(consumer)*  
**Dr. Mary Crow**, New York  
**Dr. Aileen Davis**, Toronto, Ontario  
**Dr. Peter Dent**, Hamilton, Ontario  
**Dr. Mélanie Dieudé**, Montreal, Quebec  
**Ms. Irene Driedger**, Saskatoon, Saskatchewan *(consumer)*  
**Ms. Lee Durdon**, Guelph, Ontario *(consumer)*  
**Dr. Jan Dutz**, Vancouver, British Columbia  
**Dr. John Esdaile**, Vancouver, British Columbia  
**Dr. John Fisk**, Halifax, Nova Scotia  
**Dr. Sherine Gabriel**, Rochester, Minnesota  
**Dr. Dafna Gladman**, Toronto, Ontario  
**Ms. Irene Goodale**, Caledonia, Ontario *(consumer)*  
**Dr. Esther Greenglass**, Toronto, Ontario *(consumer)*  
**Dr. John Hanly**, Halifax, Nova Scotia  
**Ms. Shirley Haslam**, Mississauga, Ontario *(consumer)*  
**Dr. Elizabeth Hazel**, Lachine, Quebec  
**Dr. Falk Hiepe**, Berlin, Germany

**Dr. Linda Hiraki**, Toronto, Ontario (*consumer*)  
**Dr. George Hiraki**, Toronto, Ontario (*consumer*)  
**Dr. Carol Hitchon**, Winnipeg, Manitoba  
**Dr. Marie Hudson**, Montreal, Quebec  
**Dr. Rob Inman**, Toronto, Ontario  
**Ms. Lori Jacobs**, Montreal, Quebec (*consumer*)  
**Dr. Sindhu Johnson**, Toronto, Ontario  
**Dr. Joachim Kalden**, Erlangen, Germany  
**Dr. Beth Karlson**, Boston, Massachusetts  
**Dr. Kevin Keen**, Prince George, British Columbia  
**Dr. Nader Khalidi**, Hamilton, Ontario  
**Ms. Claudia Lagace**, Quebec City, Quebec (*policy advisor*)  
**Dr. Carol Landolt-Morticorena**, Toronto, Ontario  
**Dr. Bianca Lang**, Halifax, Nova Scotia  
**Ms. Jaclyn Law**, Toronto, Ontario (*consumer*)  
**Dr. Ronald Laxer**, Toronto, Ontario  
**Dr. Andrew Leask**, London, Ontario  
**Dr. Allen Lehman**, Vancouver, British Columbia  
**Dr. Matthew Liang**, Vancouver, British Columbia  
**Dr. Martin Lubell**, (*Aspreva Pharmaceuticals*)  
**Ms. Cheryl Magnusson**, Vancouver, British Columbia (*consumer*)  
**Dr. Maureen Mayes**, Houston, Texas  
**Dr. Henri Ménard**, Montreal, Quebec  
**Dr. Mary Messieh**, Hamilton, Ontario  
**Dr. Paivi Miettunen**, Calgary, Alberta  
**Dr. Barbara Mittleman**, Maryland  
**Dr. Bruce Moor**, London, Ontario  
**Dr. John Mort**, Montreal, Quebec  
**Dr. Emil Nashi**, New York  
**Ms. Andrea OuHingwan**, Toronto, Ontario (*consumer*)  
**Ms. Janine Ouimet**, London, Ontario  
**Ms. Marion Pacy**, Winnipeg, Manitoba (*consumer*)  
**Dr. Pantelis Panopalis**, San Francisco, California  
**Dr. Jerry Payne**, St. John's, Newfoundland (*consumer*)  
**Dr. Christine Peschken**, Winnipeg, Manitoba  
**Dr. Ross Petty**, Vancouver, British Columbia  
**Dr. Christian Pineau**, Montreal, Quebec  
**Dr. Robin Poole**, Montreal, Quebec  
**Dr. Janet Pope**, London, Ontario  
**Dr. Rosalind Ramsey-Goldman**, Chicago, Illinois  
**Ms. Theresa Reade**, Montreal, Quebec (*consumer*)  
**Dr. Carl Richards**, Hamilton, Ontario  
**Dr. John Rioux**, Montreal, Quebec  
**Dr. Earl Silverman**, Toronto, Ontario  
**Ms. Wendy Singer**, Cote St. Luc, Quebec (*consumer*)  
**Dr. Bhagirath Singh**, London, Ontario  
**Dr. C. Douglas Smith**, Ottawa, Ontario  
**Ms. Bonnie Thorn**, Toronto, Ontario  
**Dr. Simon Tran**, Montreal, Quebec  
**Dr. Murray Urowitz**, Toronto, Ontario  
**Dr. Paul Utz**, Stanford, California

**Mr. Phil Watkins**, (*Actelion Pharmaceuticals Canada*)  
**Dr. Joan Wither**, Toronto, Ontario  
**Dr. Rae Yeung**, Toronto, Ontario  
**Dr. Sai Yan Yuen**, Montreal, Quebec  
**Dr. Michel Zimmer**, Montreal, Quebec

***Guest Speaker***

**Dr. Carolyn Bennett**, Ottawa (*Minister of State*)

***Support Staff***

**Sharon McConnell**, Toronto (*Project Manager*)  
**Luciana Brown**, Toronto (*Administrative Assistant*)  
**E. Jerry Mings**, Toronto (*Facilitator*)  
**Evelyne Michaels**, Toronto (*Science Writer*)

## **Consensus Conference on Systemic Autoimmune Rheumatic Diseases (SARD): A Research Forum on Lupus, Scleroderma, Sjögren's Syndrome, Autoimmune Myositis and Vasculitis**

### **Appendix VI About the SARD Action Plan**

To read the latest version of the SARD Action Plan, which will be updated regularly, please go to [www.sardcommunity.org](http://www.sardcommunity.org).

#### **The Action Planning Framework**

The SARD Action Planning Framework is based on the following six steps:

- 1. Identify the unmet needs** Answer the question, "What are the real, unmet needs associated with SARD?"
- 2. Identify the barriers to addressing the unmet needs** Answer the question, "What are the barriers that stop or prevent patients, researchers and academics from addressing the unmet needs of SARD?"
- 3. Identify the Strategic Directions and key strategies that will address the unmet needs** Answer the question, "In order to address the unmet needs, where should we collectively focus our efforts?"
- 4. Identify the actions to be undertaken in the next six months** Answer the question, "What are the specific actions that should be undertaken in the next six to eight months?"
- 5. List the benefits of the Action Plan to address the unmet needs.** Answer the question, "What are the anticipated benefits of the Action Plan?"

#### **SARD Action Planning Document History**

##### ***Backdated history of the SARD Action Planning Document.***

**April 11, 2006** - Work completed to incorporate feedback from Consensus Conference Co-chairs, align the action planning phase of the document, update planning document history.

**April 8, 2006** - Work completed on further clarifying the three areas of benefits (Treatment, Research and Collaboration), refining the Strategic Directions area; added a Planning Document History. The Executive Summary is pending.

**March 2006** - Working Group met to review the Action Plan Document. The Planning Model was revised to incorporate unmet needs associated with SARD and further identify specific short-term actions. The "Research Priorities" were summarized in the section "Anticipated Benefits of SARD Action Plan."

**January 2006** - Summary presentations from the SARD Consensus Conference were compiled into one Action Planning Document for review by the Working Group

**December 2005** - Consensus Conference in Toronto generates a Vision, Obstacles and Strategic Directions for SARD Research in Canada

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## Appendix VII Glossary of Terms

**Acute cutaneous lupus erythematosus (ACLE)** A type of rash that generally involves sun-exposed skin, particularly of the face. When it involves the face, this type of rash is also known as the “butterfly” or malar rash of systemic lupus erythematosus (SLE).

**Anti-DNA** Antibodies to DNA. Somewhere between one-half and 75 percent of the patients with systemic lupus erythematosus (SLE) have or will have this antibody. It usually indicates more serious activity of the disease. Although there is no one test that confirms SLE, when this antibody is found, most healthcare professionals consider it specific for the diagnosis of lupus..

**Antinuclear antibodies (ANA)** Antibodies that react to the nucleus of the cell; 96 percent of SLE patients have this antibody. However, it can be found in a small percentage of healthy people too.

**Antiphospholipid syndrome** A condition associated with specific antibodies (called “antiphospholipid” or “anticardiolipin” antibodies; also the “lupus anticoagulant”) that can lead to abnormal blood clotting or recurrent pregnancy losses.

**Anti-sense strategies.** “Antisense” drugs are based on the fact that antisense RNA hybridizes with and inactivates “messenger RNA” (mRNA). These drugs stop a particular gene from producing the protein for which it holds the code. Antisense drugs are being developed to treat lung cancer, diabetes and diseases like SARD which have a major inflammatory component.

**Apoptosis** The disintegration of cells into membrane-bound particles that are then eliminated by phagocytosis or by shedding. Also referred to as “programmed cell death.”

**Arrays** Proteins or other substances that are assembled into a format that allows analysis of multiple components in one test.

**Arthritis** Characterized by painful swelling of one or several joints. Redness and heat may be present as well. There are many different kinds of arthritis; rheumatoid arthritis and juvenile arthritis are considered to be autoimmune forms of the disease.

**Autoantibodies** Antibodies normally produced by the immune system are designed to fight infections, cancer cells and other foreign invaders of the body. Autoantibodies are unusual because they are directed against the person’s own cells and tissues.

**Autoimmune disease** A disease in which the body’s immune system attacks itself.

**Avascular necrosis (AVN)** Damage to bone caused by impaired blood flow.

**B-cell** A white blood cell that makes antibodies.

**Biological therapies** Most conventional treatments include drugs which are designed chemicals. In recent years therapies have been designed and produced as more natural components of the body (i.e. proteins). These therapeutics are referred to as “biologicals.”

**Biopsy** Removal of a small piece of tissue from an affected organ as part of the process of diagnosing a disease.

**Cataracts** Deposits in the lens of the eyes that can cause decreased vision.

**Central nervous system** Refers to the brain and spinal cord.

**Chemokines** Any of various cytokines produced in acute and chronic inflammation that mobilize and activate white blood cells.

**Chorea** Involuntary tremor or movement of arms, legs and other parts of the body.

**Chronic cutaneous lupus erythematosus (CCLE)** A skin condition that can be separate from systemic lupus erythematosus or which can be a feature of SLE. The typical lesion of CCLE is called discoid lupus erythematosus (DLE); “discoid” refers to the appearance of red, raised, scaly and disc-like patches on the skin.

**Chronic disease** A disease that lasts for a long time or for the rest of a person’s life.

**Cognitive dysfunction** Problems with memory and thought.

**Cranial neuropathies** Nerve problems related to the head and face.

**Creatinine** A chemical produced by mainly by muscles and cleared from the blood by the kidneys.

**CREST (or CREST syndrome)** A form of scleroderma; C (Calcium deposits under the skin); R (Raynaud's phenomenon); E (Esophageal dysfunction); S (Sclerodactyly –tight skin often on the fingers ) and T (Telangiectasia – a rash of tiny red blood vessels).

**Cytokines** Any of several regulatory proteins, such as the interleukins and lymphokines, that are released by cells of the immune system and act as intercellular mediators in the generation of an immune response.

**Dermatologist** A doctor specializing in skin disease.

**Dermatomyositis** An autoimmune condition that causes inflammation in the skin and muscles.

**Discoid rash** A red, raised, scaling patch of skin on the body.

**Epstein-Barr virus (EBV)** A herpesvirus that is the causative agent of infectious mononucleosis. EBV is also associated with various types of human cancers and is being studied as a potential trigger for certain SARD.

**Fibromyalgia (FM)** A condition characterized by chronic, widespread muscle pain and tenderness; fatigue is also common.

**Fibrosis** The formation of excessive fibrous tissue, as in a reparative or reactive process. It can affect the skin and/or internal organs (especially the lungs) and is seen in patients with scleroderma and rheumatoid arthritis. (see *Pulmonary fibrosis*).

**Flare** A period when an autoimmune disease is active, producing signs and symptoms.

**Galectins** A family of proteins that have been strongly implicated in inflammation and cancer.

**Giant Cell Arteritis (also called temporal arteritis)** A type of vasculitis characterized by inflammation of the temporal artery. Signs include a very high sedimentation (SED) rate, systemic symptoms, headaches and sometimes loss of vision.

**Glomeruli** Tiny filters in the kidneys that filter the blood and allow water, waste (urea, creatinine) and minerals (sodium, potassium, calcium and phosphorus) to pass through the tubes or “tubules” and out into the urine and then to the bladder.

**Glomerulonephritis (also nephritis)** inflammation of the kidneys, a potentially serious but usually treatable condition in SLE.

**Hematuria** Blood present in the urine that may have multiple causes; in a SARD patient, this can indicate that the glomeruli are not working properly.

**High mobility group box 1 protein (HMGB1)** A potent pro-inflammatory cytokine which is released by necrotic cells and triggers inflammation.

**Immunosuppressive drugs** Medications such as Cytoxan or Imuran that suppress the immune system and can be used to prevent or control symptoms or flares of autoimmune disease.

**Inflammation** The body's defence against perceived invaders. Characterized by redness, heat and swelling, inflammation occurs when white blood cells invade and surround the offending invader.

**Hypertension** High blood pressure.

**Idiopathic thrombocytopenic purpura (ITP)** Purple spots on the legs or other parts of the body caused by a decrease of the number of platelets, a blood cell that prevents bleeding.

**Immune system** The system that protects the body from foreign organisms, such as bacteria, viruses and parasites, invading your body. The system is composed of white blood cells (including T and B lymphocytes) and antibodies (made by the activation of these cells).

**Immunologist** A doctor specializing in diseases of the immune system such as allergies and SARD.

**Inclusion body myositis** An inflammatory muscle disease, characterized by slowly progressive wasting and weakness of the arms and legs. The inflammation aspect is similar to what occurs in polymyositis; however patients with polymyositis do not display many of the abnormal cellular changes seen in IBM.

**JNKs** Short for “c-Jun NH<sub>2</sub>-terminal kinases” which are involved in regulating the expression of cytokine genes.

**Keratoconjunctivitis sicca (also called xerophthalmia or keratitis sicca)** Dryness and inflammation of the cornea/conjunctiva as a result of insufficient tear production. When this symptom is found in association with xerostomia (dryness of the mouth) and polyarthritis, it suggests a diagnosis of Sjögren's syndrome.

**Lymphocytes** B and T lymphocytes are special types of white cells. Some B cells become plasma cells, which produce antibodies to fight off infection. Sometimes, these antibodies target normal tissue, causing autoimmune disease.

**Leukopenia** A low white blood cell count.

**Malar rash** A fixed red rash over the cheeks (also known as the "butterfly" rash). This rash is symmetric—on both sides of the face—with redness (erythema) and swelling (edema) of the skin over the nose and cheeks (see *Acute cutaneous lupus erythematosus*)

**Microfluidics** The science of designing, manufacturing, and formulating devices and processes that deal with extremely tiny volumes of fluid on the order of nanoliters.

**Mononeuritis multiplex** Non-symmetrical nerve involvement, causing loss of power or sensation in one or several parts of the body.

**Nanotechnology** The understanding and control of incredibly tiny bits of matter. A nanometer is one-billionth of a meter; a sheet of paper is about 100,000 nanometers thick.

**Nephrologist** A doctor specializing in kidney diseases

**Non-steroidal anti-inflammatory drugs (NSAIDs)** Drugs that decrease inflammation and can be used to control pain such as naproxen and ibuprofen. They can lead to changes in kidney function or blood pressure, and may also cause stomach ulcers. Thus, the use of these drugs should be supervised by a physician.

**Osteoporosis** Literally meaning "porous bones," a condition caused by insufficient calcium in the bones from dietary causes, disease, aging or as a side effect from taking corticosteroids or other medications. Osteoporosis causes bones to become more fragile and susceptible to fracture. *Osteopenia* is a related condition, where the bone changes are not as advanced. Both osteoporosis and osteopenia may be treated with calcium and vitamin D supplements, as well as with other drugs.

**PAMPs** Pathogen-associated molecular patterns.

**Peripheral nervous system** The nerves in the arms and legs that control movement and provide sensation.

**Photosensitivity** Skin sensitivity in which a rash develops after exposure to the sun.

**Polymyositis** An autoimmune disease of the muscles.

**Proteinuria** A protein present in the urea that indicates the kidneys are not working properly.

**PRRPs** Pattern recognition receptor profiles.

**Pulmonary fibrosis** A condition that involves scarring of the lung and is associated with scleroderma. Gradually, the air sacs of the lungs become replaced by fibrotic tissue. When the scar forms, the tissue becomes thicker causing an irreversible loss of the lung's ability to transfer oxygen into the bloodstream. Symptoms include shortness of breath, particularly with exertion; chronic dry, hacking cough; fatigue and weakness; discomfort in the chest.

**Raynaud's phenomenon** A symptom involving a change of colour (to blue, white or red) of the fingers, toes or other extremities of the body. The symptom is made worse by exposure to cold or when the person undergoes emotional stress. The colour change is related to decreased blood flow through tightened blood vessels and on occasion is accompanied by pain in the affected part.

**Remission** A period when a disease does not appear to be active or producing symptoms.

**Renal** Pertaining to the kidneys.

**Rheumatic disease** Any one of the 150 disorders that affects the immune or musculoskeletal systems; only about 30 are autoimmune in nature.

**Rheumatologist** A doctor specializing in the more than 100 types of arthritis and SARD.

**SARD** Systemic autoimmune rheumatic diseases which include systemic lupus erythematosus (SLE), Sjögren's syndrome, scleroderma (systemic sclerosis), myositis and vasculitis

**Sensory-motor neuropathy** Problems with the peripheral nervous system (*see peripheral nervous system*) that can cause problems with movement or sensation, and which occurs in a symmetrical manner.

**Sclerodactyly** A hardening of the skin of the fingers and toes seen in patients with scleroderma.

**Scleroderma (also called systemic sclerosis)** A chronic disease characterized by swelling and hardening of the skin. It is often accompanied by Raynaud's phenomenon and involvement of lungs, the gut and other organs.

**Serositis** Inflammation of a lining around a body organ, such as the lungs (pleuritis), or the heart (pericarditis).

**Schirmer test** Used to assess tear production and performed for the purpose of diagnosing and treating Sjögren's syndrome. Tiny paper tabs are inserted in the lower eyelids and removed after a few minutes. When the tab is removed, the dampened area is measured in millimetres. This helps the doctor determine the presence or extent of a dry eye condition.

**Sicca complex** Refers to the symptoms of dry eyes (xerophthalmia) and or dry mouth (xerostomia) seen in Sjögren's syndrome.

**Sjögren's syndrome** A chronic disease characterized by dry eyes, dry mouth (*sicca complex*) and abnormalities of other secretory organs. When it occurs in isolation, it is referred to as

primary Sjögren's syndrome. However, it can be accompanied by another autoimmune condition in which case it is referred to as secondary Sjögren's syndrome.

**Sulfonamides (also called sulfa drugs)** Medications best avoided by patients with SLE because they often cause a toxic reaction similar to a lupus flare.

**Synovium** A thin layer of tissue only a few cells thick which lines spaces around the body's various joints. The synovium acts to control the environment within the joint.

**Systemic lupus erythematosus (SLE)** A chronic disease with a variety of symptoms caused by inflammation in one or more parts of the body. SLE belongs to the same family of diseases that includes rheumatoid arthritis, scleroderma and other autoimmune conditions.

**Telangiectasia** Chronic dilation of groups of capillaries causing elevated dark red blotches on the skin; seen in CREST and SLE.

**Temporal arteritis (also called Giant Cell Arteritis)** A type of vasculitis characterized by inflammation of the temporal artery. Signs include a very high sedimentation (SED) rate, systemic symptoms, headaches and sometimes loss of vision.

**Thrombosis or thrombotic event** The formation of a blood clot in a vein or an artery.

**Toll-like receptors (TLR)** Receptors on cells that provide critical links between immune stimulants produced by microorganisms and the initiation of host defenses.

**Transverse myelopathy** Spinal cord inflammation or damage.

**Tumor necrosis factor (TNF)** A protein produced by macrophages in the presence of an endotoxin and shown experimentally to be capable of attacking and destroying cancerous tumors.

**Tumour necrosis factor-alpha (TNF- $\alpha$ )** It is known that over-expression of TNF- $\alpha$  acts as a driver for inflammation; this suggests that TNF- $\alpha$  inhibitors may be helpful in treating autoimmune rheumatic diseases.

**Vasculitis** The inflammation of a blood vessel wall which causes a reduction of blood flow.

**Wegener's granulomatosis** A type of vasculitis in which blood vessels become inflamed, damaging the respiratory system and kidneys.

**Xerostomia** Dryness of the mouth. When this symptom is found in association with keratoconjunctivis sicca (dry eyes) and polyarthritis, it suggests a diagnosis of Sjögren's syndrome.

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