# Background: SYRIS Design and Rationale

The following document describes the impetus and general background for SYRIS development.

**Why SYRIS? Why now? Why haven't we done this before?**

In the early years of the 21st Century, human and animal populations around the world have suffered from a bewildering and completely unpredicted panoply of new diseases of obscure origin and unknown future impact. These include SARS-Coronavirus, at least two new "bird" influenza strains (affecting humans as well), monkeypox in prairie dogs (also transmitted to humans), obvious spreading of "Mad Cow" disease in cattle in North America, and a related illness in wild and ranched elk called Chronic Wasting Disease. A pox virus of Central African primates called tanapox was reported in the U.S. in a 21-year old female recently who was back from a trip to the Republic of Congo, where she helped care for captive chimpanzees. It was only the sixth case ever reported in the U.S., and the first case in many decades.

When added to the novel emergence in the early 1990s of Hantavirus Pulmonary Syndrome in the U.S., "new variant" Cruezfeld-Jakob in the United Kingdom, the mosquito-borne illnesses West Nile and Dengue Fever, and a devastating outbreak of severe diarrheal disease in Milwaukee in 1996 due to a never-before described pathogen called Cyclospora, several clear lessons are apparent. First, there is no part of the globe that is safe from infectious disease and especially from organisms whose very existence was either unknown or thought irrelevant to human health just a few years ago. Since the vast majority of these newly described diseases cannot be treated with current medications, prevention is the only effective means of limiting the impact of these newly arrived or discovered microbes.

Second, the rapid rise in travel and the transport of exotic animals as pets or as food increases the likelihood of disease spread. Further, concentration of animals and birds in markets creates the perfect environment for organisms' adaptation to human hosts. Evolutionary biologists are fond of pointing out that "positive natural selection" is a consequence of the recombination of viral (and perhaps bacterial) genomes in novel hosts, perhaps enhancing the transmission of new influenza strains from fowl directly into human populations. It seems inevitable that new diseases, many of them fatal, will declare themselves as people inhabit previously pristine mountain and jungle habitats. The native animal species are probably also at risk, as the transmission of highly pathogenic human tuberculosis to elephants and bovine species makes clear.

Third (and hardly unrecognized) our existing public health infrastructure covering both animal and human populations is insufficiently prepared to deal with this infectious disease challenge. In part, this is due to the precipitous drop in funding for state and local public health offices (public health is a non-Federal function in the U.S., devolved long ago to counties and cities), and the complacency that followed the successful eradication of smallpox in the 1960s and 1970s, TB (almost) in the U.S. in the early 1980s, and the near universally successful vaccination campaigns against polio and measles. But there is another reason: the practice of public health remains mired in nineteenth century practices of disease-based reporting and tracking. These practices are helpful for academic dissection of disease spread and pathogenesis, but hopelessly slow if epidemics of highly communicable diseases are to be halted before large numbers of people and/or animals become ill. SYRIS is designed to provide the timely, *actionable* information that public health officials and decision-makers need in order to recognize and respond to an unusual disease outbreak at its inception before so much time has passed that intervention becomes nearly useless.

In developing SYRIS, we appreciated that physicians are trained in statistics or epidemiology, and almost none have ever had any contact with the staff of local public health offices. The vast majority of physicians, including those in primary care specialties as well as more narrowly focused practitioners, have never reported even a single case of "reportable disease" as required by law in every U.S. state and Canadian province; indeed, it is the rare clinician who can name more than a handful of the 80 or more reportable diseases that still occur in the West, let alone among recently returned travelers to exotic destinations. In the cases of human monkeypox in 2003 in the U.S., it took almost two months for the diagnosis to be made, and for the governor of Illinois to issue the necessary executive order to fully investigate and curtail the outbreak. Fortunately, monkeypox spreads poorly from human to human. Had the disease been smallpox instead (or any of a variety of other viral and bacterial-caused diseases), the tempo of this response would have proven disastrous.

Finally, for the first time in modern history, physicians, public health officials and political decision-makers have had to face the reality of bioterrorism: the intentional introduction of disease into a community. Anthrax—engineered to behave as a near-perfect aerosol—was spread by an unexpected vector, the U.S. mail, resulting in the deaths of six people and prophylaxis for tens of thousands. Millions of dollars were spent for cleanup on one Senate office building and a large urban post office, but the financial toll is still being calculated. All of this occurred as a result of a few grams of anthrax (at most), whose source is still unknown.

We also now know that multiple countries produced and stockpiled hundreds of tons of anthrax, smallpox, tularemia and plague and solved the much harder problem of creating the coating and drying techniques to enable the dispersal of these organisms from a wide variety of devices: missiles, spray tanks, bomblets and other hardware. No one knows the fate of this material. In addition, the Aum Shinrikyo cult in Japan attempted to spray anthrax into the air around their building in Tokyo; fortunately, they chose a strain of anthrax that was non-pathogenic. Had they employed the same strain as found in the anthrax laced letters to Senators Daschle and Leahy, many thousands of people may have died. And there are probably a half-dozen countries that maintain an active biological weapons program even though they are signatories to the Biological Weapons Convention that prohibits such activity.

Thus, it is likely that terrorist (or even State-sponsored) use of biological materials as weapons will continue; they may also employ novel or even genetically altered viruses and bacteria to cause disease. But, it is not necessary for terrorists to go to great lengths to find, produce, and "weaponize" recently discovered agents. Most experts believe that a few cases of foot and mouth disease (FMD) in cattle would lead to the wholesale slaughter of millions of animals in the U.S. and Canada, costing ranchers tens of billions of dollars. FMD spreads very easily from one animal to another. A few animals infected in a typical feedlot operation would quickly compromise tens of thousands of head of cattle. A few dozen cases of smallpox in North America would effectively halt transportation and commerce for months; no one knows the ultimate costs in lives and treasure, but there would be few tragedies—natural or man-made—that would rival the overall impact of such an event.

**Current public health reporting: often too late**

There is a long history in the United States of reporting diseases of public health importance to local PHOs once a diagnosis is in hand based on laboratory testing. While highly specific (that is, in most cases a positive lab test is the *sine qua non* of diagnosis in the appropriate clinical setting), the system suffers from a lack of sensitivity and timeliness. There are several reasons for this phenomenon, including the following:

- Most physicians do not know the lengthy list of "reportable diseases" in their states (there are about 80 different reporting infectious diseases, including the extremely important "vaccine preventable" diseases).
- Most physicians do not recognize classical cases of vaccine-preventable diseases simply because they have never seen a case of measles, mumps, rubella, or even chickenpox. To some extent, this unfamiliarity represents a success in eradicating much infectious disease in the United States.
- There is strong economic pressure on physicians to avoid serological diagnostic testing. In addition, samples of all types are often handled incorrectly in clinicians' offices or are compromised during transport to the lab.
- Most laboratory tests of any kind with reference to specific infectious diseases take several days to report out.

The net result is overall *clinician* compliance with regard to disease reporting is very low[1], although there is no question that if laboratories receive appropriate samples and then identify a "reportable" organism (or serological surrogate) their reporting is nearly perfect; indeed, laboratories are the backbone of disease surveillance in the US. However, even with the best of laboratory reporting, the data is received well after the patient is into the clinical course of illness (and infectiousness to others if the disease happens to be communicable).

Finally, public health officials have few, if any channels for rapidly communicating information to clinicians and other end-users of the data they have assembled and analyzed. Regrettably, there is almost no electronic alerting of physicians; even those clinicians who have computers with Internet connections (no longer uncommon) have little time to sort through the enormous volume e-mail they receive. Most physicians get their public health information from the media (television and newspapers); journal

[1] See, for example: Doyle TJ, Glynn MK, Groseclose SL. Completeness of notifiable infectious disease reporting in the United States: an analytical literature review. Am J Epidemiol 2002 May 1;155(9):866-74. For most diseases of public health importance, physician compliance with reporting requirements is less than 10%.

articles are obviously months behind any epidemic whose analysis is suitable for publication, and newsletters are not only delayed but often tossed with the junk mail that physicians receive.

SYRIS is designed to not only make it easy (little training is required) and fast (seconds) to report a case of a seriously ill patient or animal to public health officials, it also provides near instantaneous communication capability back from public health officials to clinicians and other users who can make use of important infectious disease data and analysis. SYRIS may help to improve office and Emergency Room efficiency, throughput, and cost-savings, thus encouraging clinicians to use it as part of their daily practices.

**Veterinarians: SYRIS captures cases from the Animal Kingdom**

Veterinarians see a remarkable variety of disease, if only because they have a remarkably variable clientele: many species of mammals, birds, and reptiles, both domestic and exotic (it has always amazed the author, an MD, that vets can keep all of this data organized in their minds; what veterinarians are called upon to do makes human medicine seem mundane and simple).

In designing SYRIS, we realized that there are many diseases that humans and animals share. In fact, there is a special category of diseases called "zoonoses" that refers to those infectious diseases that are more or less confined to the animal kingdom, but which occasionally affect humans. People are not "required" hosts. The infectious organism doesn't depend on people to propagate, but it will happily infect humans if it comes into contact with them (and, more often than not, kill the human in the process). Examples include: plague, tularemia, monkeypox, West Nile fever and anthrax. Indeed, it turns out that just about all of the disease-causing organisms that have been developed for anti-human biological weapons in the past (and perhaps by terrorists now) are actually primarily animal diseases in which humans are a "dead end" host (the only exception is smallpox, a uniquely human disease).

Of course, zoonotic diseases occur naturally in humans. West Nile virus (WNV) is the most recent (and most widely known) example. This virus probably entered the United States some years ago in a shipment of birds and, because it is transmitted from bird to bird by mosquitoes, it rapidly spread to domestic avian species. West Nile virus is now found everywhere in the United States and will doubtless spread to Canada, Central America and beyond. The infection is often fatal to birds, and when humans are bitten by mosquitoes carrying the virus they come down with fever and malaise (a "flu-like syndrome" in most cases) and occasionally have severe inflammation in the brain (called "encephalitis"). Thus, the presence of WNV cases among birds (and horses and even certain zoo animals like rhinoceri) is vital information for physicians. If they know the virus is circulating in the animal populations in their communities, it raises the likelihood that humans ill with fever, headache and mental status changes have WNV as the cause.

Equally important, there are many devastating infectious diseases that affect only animals. For example, foot and mouth disease is an easily communicable virus that leads to death in young calves, goats, and pigs; and weight loss (due to painful mouth ulcers and inability to eat) in adult animals. There is no treatment for the disease; most animals ultimately recover but the cost of maintaining them creates an unacceptable economic burden to farmers and ranchers, and stopping its spread becomes the first priority. Because many animals may be exposed by the time the diagnosis is made in the first victims, widespread slaughter and burning of carcasses is the only option. Early detection of infectious diseases of animals may make the difference between a small, easily controlled epidemic and a much larger outbreak that affects millions of animals (the latter occurred in the foot and mouth outbreak in the UK several years ago). SYRIS is designed to facilitate easy reporting and sharing of information among veterinarians and public health officials.

Unlike other syndrome reporting systems that attempt to utilize existing data streams, SYRIS is focused on capturing the clinical and professional *judgments* of professionals in the following communities:

- Physicians
- Veterinarians
- Nurses (especially school nurses)
- Coroners and Medical Investigators
- Emergency Medical Response teams and ambulance services
- Animal control
- Environmental health
- Clinical laboratory chemists, microbiologists, and immunologists

When clinicians see a seriously ill patient with presumed infectious disease (national studies suggest this is less than 1% of all clinical encounters in human medicine and perhaps slightly greater in veterinary practice), it takes less than 20 seconds to report that case via SYRIS. In addition, SYRIS contains summaries and analysis from local public health officials (thus focusing on diseases of importance in a particular geographic area relevant to those clinicians) that can be accessed with a single click of the mouse or tap on the PDA screen.

**Public Health analysis: Bringing it all together**

Public health officials (PHOs) serve as the "data integrators" in SYRIS. By virtue of their long experience in observing infectious disease clusters in animals and humans in their individual jurisdictions, PHOs are true experts in identifying outbreaks, and in fact determine when an "outbreak" has actually taken place. For example, a single case of measles (usually diagnosed clinically and only later confirmed by laboratory) may represent an "outbreak" in most places in the US, whereas in isolated rural villages it may be routine (and reflect the lack of adequate herd immunity from immunizations). What may be odd in one part of the country (bubonic plague in animals) is quite common in others; thus, it is the observations of clinician "sensors" combined with the analytic skill and institutional knowledge of PHOs that SYRIS brings together in one package.

SYRIS includes tools for routine statistical analysis and advanced, though simple-to-use mapping features as well. PHOs can perform near real-time overlays of various syndromes, geographic and land-use features, socio-economic data and other layers that may be of importance in analyzing disease outbreaks among animals or humans.

## A few technical comments

SYRIS is designed to run in any system environment that includes JAVA™ 1.3 (free from Sun Microsystems) or better. Examples of systems that meet this requirement are Windows 98 and better, Macintosh OS/X, Linux, and Solaris. SYRIS has been routinely tested in the Windows XP and MAC OS/X environments.

SYRIS currently operates on standard desktop and laptop computers that run Windows, Macintosh, and UNIX operating systems, and will soon be capable of operating on Palm/PDA devices. Unlike other systems, SYRIS requires no web-browser or other software; most calculations and graphics are done locally, minimizing the need for high-speed network connections and saving time. There are few, if any compatibility problems, which are common with browser-based software.

Installation is simple, and updates are automated via the Internet. The SYRIS database is maintained on a server or distributed network of servers. Information is displayed to users on a "need-to-know basis," based on factors such as user role and geographic location.

## Summary

SYRIS is a data-integration tool that gathers information of potential public health and medical importance by making reporting very fast while at the same time minimizing the burden on busy clinicians by limiting the sets of signs and symptoms ("syndromes") to a small number. SYRIS contains statistical and GIS tools that assists public health officials in rapidly analyzing the information they have received. Public health officials can update SYRIS screens in a few moments and any new analysis is immediately disseminated to all users.