

# Development and Licensing of SARS Vaccines and Immunotherapy Products: Regulatory Issues

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# Severe Acute Respiratory Syndrome : SARS

- Emergence last year of SARS in China
- Spread around the world including Canada - significant morbidity/mortality
- Major challenge to world's public health systems /considerable economic consequences
- Focus on better diagnostic and possible therapeutic and preventive measures



# SARS Immunotherapy Products and Vaccines

- Number of initiatives worldwide, including Canadian SARS Research Consortium
- **Rapid coordinated/focussed response**
- Need to facilitate the **necessary regulatory process**
- Safeguard recipients against adverse effects
- Ensure given full benefits of scientific innovation and knowledge
- Challenge ensure public safety /not to inhibit development



# Health Canada International Regulatory Workshop 18-19 August 2003

- Review data/plans, identify critical issues early on in product development
- Identify gaps which should be addressed during product development so as not to delay clinical testing and licensing
- Establish a scientific basis for making regulatory decisions concerning clinical testing and licensing



# Health Canada International Regulatory Workshop Ottawa, 2003

- Regulatory scientists, Canadian SARS Research Consortium, manufacturers of vaccines/immunotherapy products, experts in veterinary coronavirus infections/vaccines, SARS experts
- USA/Europe/Canada/Hong Kong



# International Regulatory Workshop – Ottawa, 2003

- New data – heavy viral load in many tissues from SARS patients
- Data on SARS CoV
- Immune responses IgG/IgM, including virus neutralizing antibodies, to SARS coronavirus
- New data cytokine/chemokine responses to SARS coronavirus /possible role in immunopathology



# Immunotherapy

- Vaccine very unlikely to be available for winter 2003-2004
- Passive transfer of antibodies possibility
- Use of convalescent serum or purified immunoglobulins (treatment or prevention)- limited work from Hong Kong: selection of donors difficult, ensure absence of SARS coronavirus.



# Immunotherapy

- Others opting for hyperimmune globulins from either convalescent serum or plasma from stimulated donors
- Co - development of hyperimmune globulins and vaccine
- Sera from immunized animals ( like antivenoms)



# Vaccine Development

- Several vaccine approaches, simplest inactivated SARS coV , but also recombinant proteins, live vector (adenovirus) encoding spike / nucleoproteins
- Much to be learnt from experience of veterinary coronavirus vaccines



# Vaccine Development Regulatory Issues

- Meeting emphasized that to facilitate rapid development, clinical testing and licensing use already well tried /established biotechnologies for production.
- New technologies ( cell line) would likely raise considerable regulatory issues



# Vaccine Development Regulatory Issues

- Need for Biosafety 3 production facility for coronavirus SARS CoV prior to inactivation
- Such facilities rare, may hinder development. One available in Canada
- Recent WHO guidelines for production of inactivated polio vaccine under biosafety level 3 may be helpful



# Animal Models

- Validated animal models of paramount importance – efficacy and safety – recently developed model in monkeys (Netherlands). Small animal model needed.
- Need to standardize methodologies (immune responses )



# Two major regulatory issues

- Difficulty of undertaking clinical trials to evaluate efficacy if SARS does not reappear or remains focal in nature
- Safety of inactivated SARS vaccines and immunotherapy products - fear that they will **enhance** disease.



# Two major regulatory issues: 1

- Difficulty of undertaking clinical trials to evaluate efficacy if SARS does not reappear or remains focal in nature
- Measures in place in Europe , USA and Canada to expedite the use of medicinal products where the usual requirement to demonstrate effectiveness in humans impractical



# Two major regulatory issues:2

- **Safety** of inactivated SARS vaccines and immunotherapy products - fear that they will **enhance** disease.
- Inactivated coronavirus vaccine against feline infectious peritonitis enhanced disease and death in recipients
- Certain anticoronavirus antibodies responsible



# Inactivated SARS Vaccine / immunotherapy products: safety concerns

- Early inactivated measles vaccines led to severe atypical measles with high mortality on subsequent infection
- Withdrawn from use – initial protection followed by enhancement of disease: problem lasted at least 16 years following immunization
- Respiratory syncytial virus ( RSV) similar problem



# Next Steps

- Critical regulatory issues can now be addressed in timely way
- Availability of a validated animal model for SARS of paramount importance –safety and efficacy
- New developments on global scene ?