

# BioPharm International's Virus Inactivation Series A Preface

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**B**y authoring this six-part series on “Virus Inactivation in the 1990’s — and into the 21st Century,” Gail Sofer has performed a significant service to viral safety scientists and biotherapeutic product manufacturers.

The articles in this series form a compendium of viral inactivation procedures, compiling information from several hundred articles and conference proceedings published between 1990 and 2001. A wide range of viral inactivation methods is covered here, including physical, chemical, photochemical, and irradiation-based technologies.

The methods are organized according to the type of product treated:

- tissue (skin, bone, and cells)
- blood cells (erythrocytes and platelets)
- plasma
- cell culture (media, recombinant proteins, and vaccines)
- surface disinfection, and
- experience in inactivation of specific viruses.

This series is particularly valuable in bringing together in one document the large volume of information describing in detail the virucidal effectiveness of various methodologies for treatment of numerous materials.

Issues of viral inactivation and viral transmission through blood products are extremely topical at this time. Since 1995, several new blood-borne pathogens have been identified, including the flavivirus GB virus-C/hepatitis G virus (GBV-C) and the ubiquitous human circoviruses, TT virus (TTV) and SEN virus (SEN-V) (1). Whether these viruses can cause transfusion-transmitted disease is not yet clear (2).

West Nile Virus (WNV), an avian flavivirus transmitted by mosquitoes, made its first appearance in the United States in 1999. By the end of 2002, more than 3,500 cases had been reported in the United States and Canada, with 206 deaths (3). WNV can be spread by organ donation and blood transfusion (4,5). Outbreaks of two animal paramyxoviruses — Hendra and Nipah viruses — have caused over 100 human deaths in Australia and Malaysia between 1994 and 1999. It is not known if these viruses are blood-borne (6,7).

An even more alarming pathogen — the viral agent of severe acute respiratory syndrome (SARS) — appeared in Asia in early spring of 2003 and is rapidly being disseminated throughout the globe through international air travel. The agent, tentatively identified as a coronavirus by PCR, is primarily spread by droplets but may also be airborne (8). The possibility that it has a viremic phase or can be spread through transfusion has not yet been investigated.



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Of utmost importance for the success of any pathogen inactivation method is maintaining the integrity and function of the biotherapeutic product without decreasing product stability or causing unwanted immunogenicity. Protein protectants are frequently required to minimize product damage during stressful viral inactivation treatments. Because protein stabilizers also have the potential to protect pathogens and decrease the efficacy of inactivation, careful validation of pathogen clearance in the presence of the stabilized product is essential.

Gail Sofer’s articles, collected in this issue, illustrate the need for a viral inactivation method that would reproducibly and robustly inactivate significant quantities of all types of pathogens in a wide variety of product types without causing unacceptable product damage. Toxic or mutagenic chemicals must not be part of this process. Several researchers are working to develop or optimize new methods to inactivate a broad spectrum of pathogens. One example of such a technology, fulfilling many of those requirements, is the use of gamma irradiation under optimized conditions (9). This technology allows the delivery of 50 kGy of gamma irradiation under conditions that maintain the structure and function of most biologics while inactivating large quantities of bacteria and clinically relevant amounts of both enveloped and nonenveloped viruses. We anticipate that, in the near future, this method and other advanced methods will be licensed to provide safe and effective pathogen inactivation for biotherapeutic products. This will fill an important need in improving product safety to prevent the spread of existing and emerging pathogens.

This series of articles offers an important resource for animal virologists, process engineers, regulatory experts, and those involved in developing clinical studies. Understanding the ability of specific technologies to inactivate or remove pathogens is critical in these areas. Recognizing the strong points and drawbacks of each method allows for the rational development of more effective approaches to product safety. The broad ranging and in-depth analysis of viral clearance methods presented in the current series provides a valuable tool for advancing the state-of-the art at the present time and for the foreseeable future.

## References

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