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Technical Bulletin

Microbe Selection for the SER-TAIN™ Process Validation

One of the critical aspects of designing an extraneous agent inactivation validation is the selection of specific microbes to evaluate. Those used in the SER-TAIN™ Gamma Irradiation Serum Validation were carefully selected to represent a wide range of organisms that are potential contaminants of serum products arising from either the starting material itself or from the processing environment.

When considering potential endogenous microbes in bovine serum, viruses are a main concern. Several viruses that can affect cattle are listed in Table 1, all of which are represented in the SER-TAIN™ validation.

BVD, PI_3, IBR, BTV and BLV are all bovine viral species of significant industrial importance. Although Porcine Parvovirus (PPV) does not cause disease in cattle under natural conditions, it has been isolated from bovine herds[2]. MvM was intended as a potential environmental contaminate.

Viruses of the same type and similar physical characteristics show comparable vulnerability to inactivation by gamma radiation. This allows model viruses to be used as a substitute for viruses that are difficult or hazardous to grow and titer in culture. The use of viral models in validation studies is a common practice and is recommended by the Food and Drug Administration (FDA) in evaluating the safety of human therapeutics[3]. For example, BLV is utilized in studies as a model for Human Immunodeficiency Virus (HIV).

Model viruses were also used in the SER-TAIN™ validation. Consistently propagating Bovine Leukemia Virus (BLV) *in vitro* is nearly impossible. By using Feline Leukemia Virus (FeLV), a virus that is physically similar and considerably less fastidious, the amount of protection gamma radiation provides against contamination by BLV can be accurately assessed. Based on the information gathered about PI_3 (of the family *Paramyxoviridea*), assessments can be made about the inactivation of other paramyxoviruses, such as Bovine Respiratory Syncytial Virus (BRSV). Similarly, the use of PPV as a model provides confirmation of protection against Bovine Parvovirus (BPV).

Table 1
Viruses Used in the SER-TAIN™ Gamma Irradiation Serum Validation

Virus	Family	Characteristics	Validation Virus
Bovine Viral Diarrhea (BVD)	*Flaviviridae*	ss RNA enveloped	BVD
Parainfluenza Type 3 (PI_3)	*Paramyxoviridae*	ss RNA enveloped	PI_3
Infectious Bovine Rhinotracheitis (IBR)	*Herpesviridae*	ds DNA enveloped	IBR
Bluetongue (BTV)	*Reoviridae*	ds RNA non-enveloped	BTV
Bovine Leukemia (BLV)	*Retroviridae*	ss RNA enveloped	FeLV
Porcine Parvovirus (PPV)	*Parvoviridae*	ss DNA non-enveloped	PPV
Minute Virus of Mice (MvM)	*Parvoviridae*	ss DNA non-enveloped	MvM

United States
SAFC Biosciences, Inc.
13804 W. 107th Street
Lenexa, Kansas 66215
USA
Phone +1 913-469-5580
Toll free-USA 1 800-255-6032
Fax +1 913-469-5584
E-mail info-na@sial.com

Europe
SAFC Biosciences Ltd.
Smeaton Road, West Portway
Andover, Hampshire SP10 3LF
UNITED KINGDOM
Phone +44 (0)1264-333311
Fax +44 (0)1264-332412
E-mail info-eu@sial.com

Asia Pacific
SAFC Biosciences Pty. Ltd.
18-20 Export Drive
Brooklyn, Victoria 3025
AUSTRALIA
Phone +61 (0)3-9362-4500
Toll free-AUS 1 800-200-404
Fax +61 (0)3-9315-1656
E-mail info-ap@sial.com

Non-viral contaminants from the environment, such as bacteria, fungi and mycoplasma, are also a major concern for users of serum products. Table 2 shows those organisms used in the SER-TAIN™ Validation.

Table 2
Organisms Used in the
SER-TAIN™ Gamma Irradiation Serum Validation

Organism	Type	Characteristics
Escherishia coli	Bacterium	Gram Negative
Bacillus pumilus	Bacterium	Gram Positive
Candida albicans	Fungus	Dimorphic
Acholeplasma laidlawii	Mycoplasma	Bovine specific
JH Strauss, Strain MS2	Bacteriophage	Phage 15597-B1

The bacteria and fungi species used were based on those recommended for sterility testing in the United States Pharmacopeia[4]. Although there are many types of mycoplasma, *A. laidlawii* was chosen because it is the variety that specifically affects cattle. Additionally, an *E. coli* specific bacteriophage (JH Strauss, Strain MS2) was included as a potential contaminant from the environment. The use of these organisms provides a look at the protection SER-TAIN™ processing provides against a broad range of potential environmental agents.

The unique SER-TAIN™ radiation process provides assurance against the presence of microbial contaminants in serum products. The validation of this process has been solidified by including a wide spectrum of organisms that have the greatest potential to be present in serum products and are of major industry concern. Our experience with the SER-TAIN™ process allows the validation to be expanded as new extraneous agents emerge that have the potential for transmission through bovine serum.

For more information about this subject or other SAFC Biosciences' products and services, please call our Technical Services department.

References

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2. Ibid., pg. 308.
3. "Guide To Inspections of Viral Clearance Processes For Plasma Derivatives", Federal Drug Administration Internet homepage, www.fda.gov/ora/inspect_ref/igs/viralcl.html.
4. Section 71 – Sterility Tests, United States Pharmacopeia, 1995 Edition, pp. 1686-1687.

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www.safcbiosciences.com

United States
SAFC Biosciences, Inc.
13804 W. 107th Street
Lenexa, Kansas 66215
USA
Phone +1 913-469-5580
Toll free-USA 1 800-255-6032
Fax +1 913-469-5584
E-mail info-na@sial.com

Europe
SAFC Biosciences Ltd.
Smeaton Road, West Portway
Andover, Hampshire SP10 3LF
UNITED KINGDOM
Phone +44 (0)1264-333311
Fax +44 (0)1264-332412
E-mail info-eu@sial.com

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18-20 Export Drive
Brooklyn, Victoria 3025
AUSTRALIA
Phone +61 (0)3-9362-4500
Toll free-AUS 1 800-200-404
Fax +61 (0)3-9315-1656
E-mail info-ap@sial.com