

**Risk Analysis of Classical Swine  
Fever Infectivity related to the Use  
of Porcine Spray-Dried Plasma and  
Other Blood Derivatives in Swine  
Feed**

**EAPA  
March 2004**

## Foreword

EAPA is the European Association of Animal Blood Derivatives Producer. The most of the EAPA Members started their activity during the decade of 70 to 80 with the intention to elaborated functional proteins. At that time, only ingredients used in human food were treated; later the manufacture of ingredients for pet food was started. In last years of 80 decade and beginning of 90's some of the EAPA members embarked upon a new strategy, extending its production to new and unexplored areas, and seeking additional markets.

After years of research, and in collaboration with European and US Universities, plasma was discovered as a new source of protein for use in animal feed. Plasma proteins in diets of animals offer better growth and production results when compared with milk, fishmeal or soybean proteins, as has been confirmed in research centres in Europe, America and Asia.

The aim of this study is to inform authorities responsible for food and feed safety and the consumer that any identified risks are managed in a responsible and reliable way, and in compliance with the law.

Several safety studies of this kind has been published to date, like the studies related with TSE risk and List A diseases risk analysis published by an EAPA Member, and taking account of the expertise EAPA has as European Association for the production of spray-dried blood derivatives for animal nutrition, it was considered that this document could be also contribute to the dissemination of knowledge about the industry to a wider audience.

Thus the aim of this report is threefold:

It will provide information, data and a risk analysis for the transmission of Classical Swine Fever through Porcine Blood Derivaties, analyzing the sourcing, processing, use and bio-safety of porcine spray-dried plasma and other blood derivatives for the benefit of:

- Government and other agencies concerned with regulating the bio-safety of these products, to assist them to give practical advice to the industries that use them, and to develop practical and enforceable regulations should this be deemed necessary.
- Industrial users of the product, to enable further improvement in their formulations and expand the database of knowledge for the benefit of themselves and their customers.
- Veterinary, scientific and nutritional research groups and other parties interested in the sourcing, collection, processing and use of animal-derived protein in animal feeds.

With these objectives in mind, an intercompany group was formed, consisting of experienced professionals in different fields: biologists, pharmacists, epidemiologists, nutritionists and engineers.

To maintain a scientific and objective approach, the epidemiological part of the risk assessment is following the methodology developed by the research group of Professor William Hueston and the special collaboration of Dr Kelly Rhodes of the University of Maryland in the US.

## Acronyms

AGID	Agar Gel Immuno-Diffusion
CSF / CSFV	Classical Swine Fever / CSF Virus
EC	European Commission
ELISA	Enzyme-linked Immunosorbent Assay
EU	European Union
FMD / FMDV	Foot and Mouth Disease / FMD Virus
FSIS	Food Safety and Inspection Service (United States Department of Agriculture, USA)
HACCP	Hazard Analysis and Critical Control Points system
ISO 9000	International Organisation for Standardisation - Series 9000
ISU	Iowa State University
MAFF	Ministry of Agriculture, Fisheries and Food
MAPA	Ministerio de Agricultura, Pesca y Alimentación (Spain)
OCDE	Organización de Cooperación y Desarrollo Económico
OIE	Office International des Epizooties
PRRS / PRRSV	Porcine Reproductive and Respiratory Syndrome/ PRRS Virus
QA	Quality Assurance Department
R&D	Research and Development Department
RV	Rabies Virus
UK	United Kingdom
US / USA	United States of America
USDA	United States Department of Agriculture

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## Summary

For many years plasma has been considered as an optimal protein source for animal nutrition. However, if infectious agents existed in blood there is a potential risk for the health of animals consuming these products. Furthermore if the animal diseases that theoretically may result from this practice are transmissible to humans, there is a theoretical risk to them too.

In order to determine the exact nature of the risks involved in the use of spray-dried blood products in animal feed a risk analysis has been performed. In this volume we have concentrated on possible transmission routes for infectious diseases, specifically CSF disease. This analysis has carefully investigated each stage of the spray-drying process - sourcing, processing and use of the final product - thus covering the entire process from collecting the raw material to final consumption.

Whilst processing and use are common for all geographical regions, in this study the European Union has been differentiated for sourcing, in order to take into account the specific animal disease risks associated with this region. The status of the region as determined by the OIE in relation to the CSF disease has also been taken into account.

In conclusion, it can be said that porcine spray-dried blood derivatives, and specifically porcine spray-dried plasma, should be considered as safe and of minuscule to remote risk for transmission of CSF disease so long as they are harvested, processed and used as recommended in this document.

## Key Words

Risk Assessment, Safety, Spray-drying, Porcine spray-dried plasma, Animal feed, Animal blood, Plasma, OIE List A diseases, Classical Swine Fever, CSF, *Ante mortem* examination, *Post mortem* examination, EU.

# 1 Introduction

Public concern for food safety has been, and continues to be, of major importance, both for the industry and government agencies involved in regulating the safety of food and feed. Since many foods are directly derived from animals, the health of such animals is of fundamental importance when considering the safety of food derived from them. As a Association involved in the production of ingredients for human food and animal feed, EAPA Members remains dedicated to the production of safe and nutritional products, for both humans and animals. For the past 15 years, EAPA Members has been devoted to using the natural nutritional benefits of blood and blood derivatives, whilst remaining aware at all times of the need to assure the safety of such products. The company members have continued to improve and develop its processes and products through extensive research and analytical assessment to ensure quality and safety. Before the animal protein ban, more than 150 million piglets per year were being fed with the proteins produced by EAPA Members and other Blood Producers. Actually the use of blood derivatives for swine nutrition is extensively extended in third countries of America, Asia and East Europe.

EAPA Members have carried out extensive testing and research to determine the potential risks with its products, and the best way to reduce these risks. The members remains open and willing to review and discuss any data in reference to the results and conclusions presented in this assessment.

In this report the processes involved in the production of porcine spray-dried plasma intended for swine consumption have been reviewed and analysed. Whilst there are many safeguards used to ensure that animal diseases of concern are reported prior to shipment to slaughtering facilities, the focus of this study is on processing. That is *ante mortem* and *post-mortem* inspection, collection of the raw material, separation, cooling, transport, processing leading to the eventual spray-drying, and analytical evaluation of the finished product.

A qualitative risk assessment model is used.

Throughout the past 15 years of industrial experience in producing blood products and their derivatives for animal consumption, there has not been a single documented case of animal disease attributed to spray-dried blood products prepared by EAPA Members or other blood producer and used in animal feed.

In addition, improvements have been made over the years in collection facilities, filtration and chilling, which have further reduced or minimised the risks, as well as improving the nutritional quality of the products.

The animal blood processing industry has not received much attention, and the processes and safety measures used are not well-known by government officials and experts in animal health. This assessment is being presented so that spray-dried blood products are recognised not only as highly nutritional feed ingredients, but also for the economical and environmental importance of recovering this valuable resource.

EAPA members frequently draws an analogy between blood products and powdered milk or eggs, in that they are all high in protein, nutritionally preserved and processed with very similar equipment and methods.

The aim of this report is to present constructive information regarding processing and the products resulting therefrom, along with an evaluation of risks and the measures taken to reduce them.

This report is written according to following structure:

The document starts with the presentation of the model used for the risk assessment, followed by the processing steps, from the collection of the raw material to the final use of the product. The report only address the potential risk of spreading CSF disease through porcine blood products, that may from time to time be present in each of the European countries.

Finally a review of the Quality Assurance systems and information channels systematically used by EAPA Members to manage potential hazards is included.

## **2 Application of the Risk Analysis Paradigm The Safety of Porcine Spray-Dried Blood Derivatives for Animal Consumption in relation to the CSF risk of transmission.**

### **2-1 Introduction**

Blood derivatives, such as spray-dried plasma from swine, have been identified as valuable and safe feed ingredients for newborn piglets and other livestock. Although no case of contamination from ingestion of feed with spray-dried blood derivatives has been reported, whole blood is known to transmit a number of important diseases through insect vectors and contamination of instruments and equipment. Diseases of particular concern are those found in List A of the Office International des Epizooties (OIE), i.e.:

transmissible diseases which have the potential for very serious and rapid spread, irrespective of national borders, which are of serious socio-economic or public health consequence and which are of major importance in the international trade of animals and animal products.<sup>5</sup>

Manufacturers of blood derivatives have a vested interest in determining the safety of their products for use in animal feeds. The safety of spray-dried blood derivatives can be evaluated through a systematic consideration of blood sourcing, harvesting, processing, packaging, distribution, and the final use of the products in animal feeds. Risk analysis tools have been used to identify the potential hazards, compile the relevant data and estimate any risk of disease transmission. This report serves to summarise the overall safety evaluation of porcine spray-dried plasma with regard to the CSF disease.

### **2-2 Application of Risk Analysis Paradigm to Evaluate the Safety of Animal Feed Ingredients**

Risk analysis consists of a set of tools for rational decision-making using the best scientific evidence available. It provides a systematic strategy for evaluating specific processes and products for potential transmission of animal diseases. Consequently, the risk analysis paradigm is a logical approach to considering the safety of spray-dried blood derivatives used in animal feeds.

Risk analysis has four components: hazard identification, risk assessment, risk management and risk communication. While every risk analysis embodies all four of these components, they most commonly occur

concurrently rather than in sequence. Risk analysis is applied to the systems model of the product, i.e. raw material sourcing, processing and end product usage.

### **2-2-1 Hazard Identification**

The foundation of risk analysis is a systematic consideration of ‘what can go wrong?’ and ‘how would it happen?’ The identification of hazards examines each of the steps in the manufacturing process and use of the feed ingredient, from the sourcing of raw materials to the formulation and consumption of the final feed. A flowchart of the manufacturing process can provide a visual representation of both the potential hazards and the specific point at which they might occur. All risk analyses incorporate some form of hazard identification.

### **2-2-2 Risk Assessment**

Once the potential hazards are identified, the risk assessment addresses the questions of ‘how likely are things to go wrong?’ and ‘what are the implications should they go wrong?’ Risk assessments of disease must examine the unique characteristics of each potential pathogen, such as the likely exposure of the population, minimum exposure dose needed to cause disease, and the immune status of those animals exposed. The risk assessment can use qualitative or quantitative estimates of risk, depending on the quality of the data available and the needs of the risk assessor. Qualitative risk assessments are the most frequently used approach, summarising the likelihood and implications of the hazard in terms such as remote, small, or significant.

### **2-2-3 Risk Management**

Risk management focuses on the options available to reduce the likelihood of the hazard occurring, or the implications should something go wrong. Consideration of risk management allows for comparisons of various alternatives in terms of both their feasibility (and cost) and effectiveness. From a risk management perspective, reduction of the overall risk or implications can derive from any of a number of different prevention steps. Using the systems model, management of risk at any stage of sourcing, processing, or use may obviate the need for risk management at other steps. In other words, if the raw material carries no hazards, then the effectiveness of processing is moot unless cross-contamination occurs. Similarly, if the processing effectively inactivates the disease agent or the final product use is not associated with disease transmission, then the disease status of the raw material is not important. In reality, effective risk management strategies

usually target multiple control points along the sourcing-processing-use continuum.

#### **2-2-4 Risk Communication**

All of the potentially affected parties can contribute valuable input to risk analysis. Risk communication is the two-way process of soliciting input and sharing progress while the risk analysis is underway. Establishing effective channels of communications is also critical to achieving the recognition that risk analysis is a continuous process, which must be reconsidered as new data becomes available or situations change.

### **3 Risk Assessment for the risk of CSF Virus transmission through Porcine Blood Derivatives in Piglets.**

This qualitative risk assessment examines the risk of an individual animal being exposed to CSFV through consumption of porcine spray-dried plasma. The theoretical risk of exposure exists because blood is initially derived from swine originating from countries in which this disease may exist. This assessment is separated into four sections that correspond to the chain of production: animal sourcing, blood harvesting, blood processing, and end product use. Under each section a number of risk factors will be assessed.

In order to assess the risk of an individual animal being exposed to infective CSF Virus through consumption of porcine spray-dried plasma it is necessary:

- to establish the CSF disease status of the region (EU) and/or herd of origin from which the animals are sourced
- to establish the risk the slaughter animals have of harbouring an CSF infectivity.
- to establish the inherent risk of disease transmission associated with blood for CSFV
- to establish whether the slaughter or blood harvesting procedures increase or decrease the risk of the end product containing infectivity of CSF
- to establish whether blood processing increases or decreases any infectivity of the CSF Virus present in the raw material
- to establish how the use of the final product affects the likelihood of disease transmission to an animal should infectivity of the CSF be present in the finished product

Given the fact that 'zero risk' does not exist, the five basic risk categories and their definitions are:

Minuscule	Extremely small or hypothetical risk of infectivity being present.
Remote	Very little risk of infectivity being present.
Low	Some small risk of infectivity being present.
Significant	Definite risk of infectivity being present; exposure.
Massive	High likelihood of infectivity being present and exposure likely.

A basic level of risk (minuscule, remote, low, significant, or massive) is assigned to the raw blood at sourcing; steps in harvesting, processing and use are evaluated as either increase, decrease, or no change in overall risk. The end of each section contains a summary of risk encompassing both inherent risks and evaluation of risk management strategies.



## **a) Animal Sourcing from the European Union**

### **1 Risk Factor: Countries of Origin of Slaughtered Animals**

Quarantine control on live farm animal transport between EU Member States has been removed, and border checks are no longer applicable to such trade. This greater freedom of animal movement presents extra risks regarding the animal health status of each member state, so that an OIE List A disease present in any one Member State may contribute to risk in another. For the purposes of this assessment, the entire EU will be treated as if it were one unit, with breakdown to country level where appropriate.

#### **1-1 Issues of Concern (Country of Origin)**

Factors to consider when assessing the risks involved with sourcing from any country:

the status of that country for CSF disease, the CSF disease surveillance system, the veterinary services within the country, and the laws and regulations regarding suspect animal reporting within the country

The status of a country for CSF is determined on the basis of criteria described in the International Animal Health Code of the OIE.<sup>1</sup> Criteria of importance as outlined by the OIE are summarised below.

##### **1-1-1 Specific Disease-Free Country**

For the purpose of this assessment, a country may be considered free of a particular List A disease when the following conditions are met:

the disease is notifiable in the country and record-keeping confirms regular and prompt disease reporting where applicable, and appropriate disease control measures as specified by the OIE are followed in the case of importation of live animals, semen, embryos/ova, and animal products, and no clinical, serological, or epidemiological evidence of the disease has been found during a specified period of time determined by the OIE, which may be one, two, or three years depending on the disease.

In point outbreaks of certain diseases a stamping-out policy may be practised which decreases the above period.

### **1-1-2 Specific Disease Infected Zone**

There are few situations nowadays in which an entire country is affected by an OIE List A disease. Strict surveillance and control of these economically devastating diseases usually diminishes the affected area within a country to an 'infected zone'. These are areas in which there is, or has recently been, clinical or epidemiological evidence of a particular List A disease. Clearly a country in which there is an infected zone cannot be considered free of that particular disease. Conversely, regionalisation may allow the infected zone to be delimited so that the rest of the country can be considered free.

### **1-2 EAPA Members Process Description**

EAPA Members contracts with pigs slaughterhouses in the EU: Belgium, Denmark, France, Germany, Holland, Italy, Sweden, Spain, and UK. Slaughtered animals originate from the surrounding regions. All List A diseases are reportable in each participating country, meaning that both the attending veterinarian and the diagnostic laboratory involved are required to report their findings immediately to appropriate regulatory officials. These include National Minister at the level of the member state, and SANCO of the European Commission.

In EU, the CSF is a notifiable disease according to the Council Directive 82/894/EEC, and the Community measures for the control of CSF are compiled in the Council Directive 2001/89/EC

Importation of live animals, semen, embryos/ova, and animal products into member states of the EU occurs in accordance with disease control measures outlined by the OIE International Animal Health Code and the previously mentioned Council Directive 2001/89/EC. No clinical, serological or epidemiological evidence of Classical Swine Fever (CSF) has been found in the EU in the recent past, except one outbreak notified in Slovakia according with the Animal Disease Notification System (ADNS) from EU Members State. EU Member States are therefore considered free of CSF disease<sup>2</sup>. For reasons previously mentioned, this assessment will continue to generalise risk to the level of the entire European Union.

There have been several outbreaks of CSF in Europe during the recent years. During an official outbreak of CSF in a farm, following the EU and OIE rules is mandatory put the farm in quarantine and all living pigs need to be destroyed. Control measures included establishing a zone at risk, with standstill and testing of all animals.

In 2003 several EU Members State (Belgium, France, Luxemburg, Germany, Italy and Austria) notify the presence of this disease, in some cases only in wild boar. All living domestic pigs were destroyed in accordance with European regulations, and to date there has been no evidence of further disease spread.

### **1-3 Analysis of EAPA Member Process (Country of Origin)**

Clearly no stipulation exists that states that slaughtered animals originate from a country of origin or zone free of CSF disease. CSF outbreaks have occurred sporadically in several EU member states, but are quickly contained and stamping out policies pursued. Control and surveillance measures at the country level and higher, limit the overall risk of CSF disease in porcine plasma sourced from the EU.

### **1-4 Country of Origin Score: Low**

## **2 Risk Factor: Herd of Origin**

### **2-1 Issues of Concern (Herd of Origin)**

Herd level documentation may provide a more specific degree of surveillance than reliance on countrywide regulations alone.

### **2-2 EAPA Members Process Description**

Source animals are from the open population in the area serviced by each slaughterhouse. The slaughterhouses are located within reasonable geographical distance of the processing plants. Specific herd level health status documentation is not required for swine, although each slaughterhouse maintains records and can trace a shipment in aggregate back to the original farm.

### **2-3 Analysis of EAPA Members Process (Herd of Origin)**

Information at herd level is available from the farm and can be tracked by EAPA Members through the slaughterhouse. However, CSF, is reportable to both national regulatory officials and EC, and measures are in place to contain or destroy susceptible animals in the area of an outbreak.

Geographical distance may limit risk since slaughterhouses are in countries currently free of CSF disease, but this cannot be guaranteed.

### **2-4 Herd of Origin Score: Potential to Reduce Risk**

***Note:** Geographical distance may reduce risk of animals originating from an infected herd presenting for slaughter. No other EAPA Members risk management occurs with regard to herd of origin.*

## **3 Risk Factor: Individual Source Animals**

### **3-1 Issues of Concern (Individual Source Animals)**

#### **3-1-1 Species Affected**

CSF affect swine only. CSF in wild boar causes difficulties for controlling this disease in the European Union.

#### **3-1-2 Clinical History**

Asymptomatically infected animals are an important means of CSF spread since chronically infected animals can shed CSF virus continuously or intermittently for life.<sup>3</sup> Asymptomatic infections can occur in a herd without any clinical cases if a low to moderately virulent strain of CSF is introduced, although this is rare in an established herd.<sup>4</sup> All List A diseases spread to other susceptible animals, therefore multiple affected animals in a herd are more common than individual cases. A complete clinical history provides supporting evidence of infection.

#### **3-1-3 Laboratory Testing**

Serological tests prescribed by the OIE and the EC to confirm the diagnosis of CSF are fluorescent antibody virus neutralisation, ELISA, or neutralising peroxidase-linked assay.

#### **3-1-4 CSF Disease Exposure Status**

Residence of a source animal within quarantine area or restricted zone constitutes a high degree of potential exposure to CSF disease. Conversely, residence in any country or area currently free of a particular disease implies very little probability of exposure.

### **3-2 EAPA Members Process Description (Individual Source Animal)**

Slaughterhouses contracting with EAPA Members collect blood from swine brought in from the open population of the surrounding area, without regard to clinical history, laboratory testing, or exposure status. All animals continuing to slaughter must pass an *ante* and *post mortem* inspection that excludes animals showing clinical signs of disease.

### **3-3 Analysis of EAPA Members Process (Individual Source Animal)**

EAPA collects blood from swine that have passed *ante mortem* examination (see **Harvesting, Section 1-1-2**).

### **3-4 Individual Source Animal Score: No Impact on Risk**

## **4 Risk Factor: Disease Characteristics**

### **4-1 Issues of Concern (Disease Characteristics)**

#### **4-1-1 CSF Disease Characteristics**

By definition the CSF (OIE List A) disease is transmissible and spread rapidly, hence disease usually affects multiple animals rather than the isolated, sporadic case. Consequently, CSF disease is well suited for active and passive surveillance programs where an adequate veterinary infrastructure and diagnostic laboratory system exist. The exception is those diseases in which sub-clinical or asymptomatic infections can occur in a group of animals without overt clinical signs in any one animal. CSF and other List A diseases occasionally occur in this fashion, but this is unlikely in an established herd<sup>4</sup> - this is the exception rather than the norm.

#### **4-1-2 Incubation Period**

The incubation period of a disease is the time between initial infection and onset of clinical signs. During this time the infected animal may appear clinically normal, and the disease may or may not be detectable by laboratory testing. An infected animal incubating CSF may carry the causative agent in the blood and may also shed small amounts in bodily secretions. The incubation period of CSF is approximately 2-14 days.<sup>2</sup>

#### **4-1-3 Sub-clinical Illness or Asymptomatic Infection**

In sub-clinical illness or sub-acute infection, signs of disease are mild to asymptomatic. The infected animal may appear clinically normal, and the disease may or may not be detectable by laboratory testing. These disease states play an important role in the propagation of several List A diseases. Asymptomatic infection is non common in CSF.

#### **4-1-4 Chronic Carrier State**

A chronic carrier state exists when an animal has passed through sub-clinical or clinical infection and recovered without ridding itself of the infectious organism. Chronic carrier animals are particularly important for the persistence of disease and its spread to new areas. Although a carrier state plays an important role in several List A diseases, it is an important means of CSF spread.

#### **4-2 EAPA Members Process Description (Disease Characteristics)**

Blood is collected from swine that pass *ante* and *post mortem* inspection at participating slaughterhouses. No additional testing is conducted to detect possible incubation state, sub-clinical illness, sub-acute infection, or chronic carrier status.

#### **4-3 Analysis of EAPA Members Process (Disease Characteristics)**

No information is available about the disease or exposure status of individual animals that do not display clinical signs.

#### **4-4 Impact of Disease Characteristics: Potential to Increase Risk**

### **5 Risk Factor: Tissue Type**

#### **5-1 Issues of Concern (Tissue Type)**

Individual tissues vary in their potential for OIE List A disease infectivity. The tissue of interest here is blood, specifically the presence of a CSF agent in the blood of an infected animal.

Items to consider when evaluating the risks involved with blood include:

- whether that agent is present in the blood of an infected animal
- at what stage of disease viraemia or bacteraemia occurs
- the length of time viraemia or bacteraemia persist
- virus or bacteria titers achieved in blood at various stages of disease from incubation to clinical signs
- infectivity of the agent in blood

Transmission of CSF is primarily by direct contact, fomites, and swill feeding; there is no evidence supporting an arthropod vector. The CSFV initially infects the epithelial cells of the tonsillar crypts and subsequently spreads to the regional lymph nodes through lymphatic vessels. It is then transported in the peripheral blood and on to secondary sites of replication.<sup>5</sup> The duration of viraemia is unknown, although carrier animals can shed CSFV continuously or intermittently for life.<sup>3</sup>

## 5-2 EAPA Members Process Description (Tissue Type)

Same as above (see Section 4-2)

## 5-3 Analysis of EAPA Process (Tissue Type)

CSFV are present in the blood of infected animals at some point during the course of disease. EAPA Members establishes no risk reduction measures associated with viraemia at the time of collection beyond *ante* and *post mortem* inspection and sanitary collection procedures. Tissues other than blood are not collected. Tissue type increases risk for CSF virus since the virus could be isolated from the blood of infected animals, but this possibility is less clear regarding the evident symptoms in infected animals.

## 5-4 Tissue Type Score: Increases Risk

# 6 Summary of Blood Sourcing

**Table 1: Summary of Risks Associated with Blood Sourcing from the EU**

<b>RISK FACTOR</b>	<b>GRADE</b>	<b>COMMENTS</b>
Country of Origin	Low	Control strategies at country and EU level limit CSF
Herd of Origin	Potential to Reduce Risk	Geographical distance may limit risk
Individual Source Animal	No Impact on Risk	
Disease Characteristics	Potential to Increase Risk	Existence of sub-clinical or incubating cases increases risk if disease present
Tissue Type	Increases Risk	CSFV are present in the blood of infected animals
Overall Source Risk	Low	

There is a low risk that raw blood sourced from slaughterhouses in the EU to be processed for animal consumption will contain CSF disease infectivity. The main factors influencing this assessment are the low inherent risk associated with the countries of origin given the location of the processing plants and the aggressive disease surveillance and control programs in place for CSF at country level and higher. Individual animals must pass *ante* and *post-mortem* examination. Chronic carrier animals may increase risk if CSF is present in the pig population.

## **b) Harvesting – CSF Virus**

### **1 Risk Factor: General Considerations**

#### **1-1 Issues of Concern (General Considerations)**

##### **1-1-1 Quality assurance/Quality control**

Quality control/assurance programs strive to monitor procedures related to important issues of concern. Internationally recognised methods of quality standardisation, such as ISO 9000, help to ensure that methods implemented to reduce or control the transmission of infectious agents are consistently adhered to during the slaughter process. Limiting the number of 'high risk' procedures or variables within the slaughter process may serve to further reduce the risk of transmitting infectious diseases should they be present.

Some variables include:

- use of a dedicated facility
- limiting the number of species slaughtered during a production run
- the use of dedicated personnel for collection of tissues of interest
- standard operating procedures for the collection of tissues of interest

Inspections by government authorities may serve as a measure of quality control at country level. Facilities regularly inspected should retain records of certification by these agencies as evidence of compliance with guidelines established for the collection of bovine derived materials.

##### **1-1-2 *Ante mortem* Examination**

All advanced meat inspection regulations specify the need for an examination of the live animal, for public health protection and promotion of animal health. The main purpose of *ante mortem* inspection is to separate normal and abnormal livestock. Normal animals are sent forward to slaughter, while animals found to be affected by some abnormal condition are either immediately condemned or retained for further inspection. Condemned animals do not enter the slaughter facility but rather are separately treated for a specific disease or disposed of under supervision of the inspector. Suspect animals may subsequently be condemned or passed for slaughter under special precautions. Suspect animals sent for slaughter are clearly marked and accompanied by a full veterinary report, and are subjected to a rigorous *post mortem* examination.

Current *ante mortem* inspection practices should exclude clinically ill animals, but may not definitively detect animals that are incubating disease, sub-clinically ill, or chronic carrier animals. Chronic carrier animals may be

condemned on *ante mortem* inspection for signs of disease arising from their carrier state (i.e. emaciation, pneumonia), but not suspected of harbouring a CSF disease. In the unlikely event that an animal showing clinical signs of a CSF presents for slaughter, that animal would be condemned on *ante mortem* inspection.

Agriculture and Agri-Food Meat Inspectors or equivalent trained technicians perform *ante mortem* and *post mortem* inspections

### **1.1.3 Post mortem Inspection**

The acute form of the disease, which is the most frequent form, shows very clear clinical signs that appear shortly after the infection. Other forms such as sub-clinical, chronic or congenital are more difficult to diagnose.

Most gross lesions in acute CSF result from viral damage to blood vessels, leading to inflammatory haemorrhage in the skin, larynx, bladder, brain, and kidneys. Haemorrhage in the latter produces a characteristic 'turkey egg' appearance. Blood vessel damage in the intestines results in haemorrhage and circular 'button ulcers' around the ileum-cecal junction. In chronic cases hemorrhagic inflammatory lesions are often absent: there is a generalised depletion of lymphoid tissue, but this may be hard to appreciate on gross examination.<sup>4</sup> Necrotic ulceration of the large intestine is common, and transverse calcification of the distal portion of the ribs may be seen.<sup>6</sup>

Nevertheless, it is important to take into account that, during the outbreak of CSF in Spain (1997-98) an EAPA Member analysed more than 150 batches of spray-dried blood derivatives, both with serological and tissue culture methods. The results of all these analyses showed the absence of infective particles in all the batches analysed.

## **1.2 EAPA Members Process Description (General Considerations)**

EAPA Members has contracted with multiple slaughterhouses in the EU for the collection of blood. Slaughterhouses are routinely inspected by the proper regulatory officials. Collection of blood derivatives in the EU occurs in accordance with European legislation (92/5/EEC or 1774/2002/ EC).

Each slaughterhouse follows standard operating procedures for draining carcasses and collecting blood, and personnel are trained in these procedures as part of the quality assurance program. The collection of blood is performed during routine production runs. Each slaughterhouse collects blood from only one species or in independent and geographical separated slaughter lines.

### **1-3 Analysis of EAPA Members Process (General Considerations)**

A documented quality assurance program is in place for the collection of blood; a shipment of plasma can be traced back to a group of farms from which the blood must have come; and an official *ante* and *post mortem* examination supervised or conducted by official veterinary surgeons under the jurisdiction of the competent veterinary authority is in place for all animals entering the slaughterhouse. Slaughterhouse standard operating procedures for quality assurance regarding the collection of blood ensure proper handling.

### **1-4 General Considerations Score: Reduces Risk**

## **2 Risk Factor: Tissue Collection**

### **2-1 Issues of Concern (Tissue Collection)**

#### **2-1-1 Stunning**

After passing *ante mortem* examination, the animal is stunned prior to bleeding.

#### **2-1-2 Exsanguination and Initial Collection**

Blood is collected shortly after the animal is stunned and suspended on the slaughter processing line. Ideally, collection takes place at a stage in which there is minimal opportunity for exposure of the blood to higher risk materials, therefore limiting the potential for cross-contamination. Combining or pooling of tissues from multiple source animals increases the risk that any given collection will contain a CSF infectious agent. However, pooling from multiple sources may result in a significant dilution factor and this may decrease overall infectivity provided that subsequent multiplication of an infectious agent is minimised.

#### **2-1-3 Preservation and Anticoagulation**

Prevention of clot formation is important with regard to maintaining homogeneity of the blood prior to separation of the blood components and promoting the dilution factor.

## **2-2 EAPA Members Process Description (Tissue Collection)**

Stunning and slaughter (bleeding) procedures are performed in accordance with the regulations of each country according with the EU Regulation, typically disclosed in a document governing animal handling, restraint, methods of stunning and slaughter, and control of the process through quality assurance programs.

Principal stunning methods of swine in EU are either Electrical or CO<sub>2</sub> .

After stunning, the animal is suspended on the slaughter line by one or two hind legs or laid on one side, the jugular veins and carotid arteries are severed, and the animal bleeds out into a collection trough. Blood from multiple animals is collected in a common trough. Prior to collection, the trough is sprayed with citrate/sodium phosphate, a preservative and anticoagulant commonly used in the collection of blood.

## **2-3 Analysis of EAPA Members Process (Tissue Collection)**

Blood is collected during the killing of the animals, just after suspension on the slaughter line. Therefore collection occurs prior to the opening of the carcass, with minimal opportunity for cross contamination from other tissues. Sources of potential contamination include the hide and the oesophagus (which may be severed along with the jugular veins). Collection of blood from multiple carcasses into a common receptacle both increases risk of contamination of an entire batch from one diseased animal and conversely dilutes potentially infectious agents. Citrate/sodium phosphate effectively retards clotting of the blood.

## **2-4 Tissue Collection Score: Potential to Increase Risk\***

*\* The dilution effect also can contribute to reduce the risk in some cases.*

# **3 Risk Factor: Post-Collection Handling**

## **3-1 Issues of Concern (Post-Collection Handling)**

Shortly after collection blood is centrifuged to separate plasma and cells, then each component is separately stored. Raw fluid materials are handled carefully, in a dedicated closed system to prevent contact with any contaminated carcass or associated equipment. Use of storage tanks dedicated to blood or blood products from one species only is the norm. Specially trained personnel should be assigned to the blood separation and storage process, and training should be based on standard operating

procedures developed to address disease risks associated with blood derivatives. Minimal or no replication of CSF viruses occurs in the absence of life, so there is little risk of a viral agent multiplying due to inadequate storage facilities or shipping conditions.

### **3-2 EAPA Members Process Description (Post-Collection Handling)**

The blood collected is centrifuged either at the slaughterhouses directly after collection or at the manufacturing plant. Blood or plasma is transported via a closed system to stainless steel storage tanks and held at refrigerated temperature until shipment. Blood or plasma from multiple collections is combined in one tank. Blood or plasma from several slaughterhouses may be combined in one storage tank at the plant. In a few slaughterhouses whole blood is stored in dedicated tanks and hauled to a central facility where centrifugation occurs.

### **3-3 Analysis of EAPA Members Process (Post-Collection Handling)**

Measures to ensure minimal likelihood of cross-contamination have been established. Once again, pooling of blood products from multiple source animals is not ideal with regard to overall contamination, but the serial dilution factor is advantageous in reducing overall infectivity per unit blood. A storage refrigerated temperature does not reduce risk since several OIE List A disease agents persist at that temperature<sup>3,7</sup>, although refrigeration during storage and shipment maintains the integrity of the plasma product. Effects of centrifugation will be addressed under Plasma Processing.

### **3-4 Post-Collection Handling Score: Potential to Increase Risk\***

*\*The dilution effect also can contribute to reduce the risk in some cases.*

## 4 Summary of Harvesting

**Table 2: Summary of Risks Associated with Harvesting – EU**

<b>RISK FACTOR</b>	<b>GRADE</b>	<b>COMMENTS</b>
Sourcing Score	Low	See ' <b>Sourcing</b> '
General Considerations	Decreases Risk	<i>Ante</i> and <i>Post mortem</i> inspection removes clinically affected animals
Tissue Collection	Potential to Increase Risk	Pooling blood may increase risk
Post-Collection Handling	Potential to Increase Risk	Pooling plasma may increase risk
Cumulative Score Post-Harvesting	Low	

There is a low risk that blood harvested from slaughterhouses in the EU will contain CSF infectivity. The main factors influencing this assessment are the low risk associated with sourcing, the *ante* and *post mortem* inspection regulations pertaining to slaughter, and the dichotomous impact of pooling blood or plasma.

## **c) Plasma Processing – CSF Disease**

### **1 Risk Factor: Concentration**

#### **1-1 Issues of Concern (Concentration)**

##### **1-1-1 Centrifugation**

Citrated blood is centrifuged to separate plasma and cells, ideally soon after collection. Since the resulting plasma is of much smaller volume than the original blood, centrifugation may result in a higher dose of infectious agent per unit volume if present. Several OIE List A disease agents are cell associated, and so the risk of such agents in the final product is diminished by removing the cells and some cellular debris.

##### **1-1-2 Vacuum Evaporator or Reverse Osmosis and Nano-filtration**

After centrifugation, and prior to spray-drying, the plasma is subjected to concentration by vacuum evaporator or by reverse osmosis and/or nano-filtration. These last processes involve the use of membrane systems to filter out undesired mineral content and water, thus concentrating the plasma components.

#### **1-2 EAPA Members Process Description (Concentration)**

Centrifugation occurs shortly after collection, in some cases while still in the slaughterhouse, although in other collection facilities chilled whole blood leaves the slaughterhouse and centrifugation occurs at the plant. The blood cells are disposed of by either the slaughterhouse or the plant, and are treated separately. In some cases the blood cells are used as raw material for the production of blood meal, in other to obtain a meat colorant for meat industries and in others are spray dried in strong temperature conditions that spray dried animal plasma

#### **1-3 Analysis of EAPA Members Process (Concentration)**

Centrifugation may also reduce risk of CSFV since this virus tends to remain largely entrapped in infected cells outside of the blood.<sup>7</sup> It has been noted, however, that CSFV<sup>7</sup> can be transmitted in a cell-free filtrate of blood. Reverse osmosis and nano-filtration are not effective in reducing risk and may even serve to concentrate CSFV in raw plasma. Processing proceeds quickly from collection to spray-drying.

## **1-4 Concentration Score: No Impact on Overall Risk (EU,)**

## **2 Risk Factor: Spray-Drying**

### **2-1 Issues of Concern (Spray-Drying)**

The spray-drying process subjects plasma and any viral contaminants to extremes of heat and desiccation, as well as high pressure. In general, viruses are more sensitive than bacteria or fungi to inactivation by temperature and other physical or chemical agents.<sup>8</sup> Factors to consider include the effects of pressurisation, time and temperature on virus inactivation, as well as the degree of homogeneity in size and consistency of plasma droplets achieved.

#### **2-1-1 Particle Homogeneity**

It is important for consistency of drying that the sprayed droplets are homogeneously sized and arrive at a consistent rate so that all particles are exposed to the same temperature conditions. Failure in this respect could result in incomplete drying and persistence of a disease agent.

#### **2-1-2 Pressure**

viruses are generally sensitive to considerable changes in the physical environment.<sup>8</sup>

#### **2-1-3 Temperature**

Animal viruses vary considerably in regard to heat stability. Surface proteins are denatured within a few minutes at temperatures of 55-60°C, with the result that the virus is no longer capable of normal cellular attachment and/or uncoating.<sup>8</sup> Inactivation progresses more rapidly as temperature rises: the half-life of a virus can be measured in seconds at 60°C, minutes at 37°C, hours at 20°C, and days at 4°C. The exact time/temperature curve of inactivation is specific to each virus.

Little information is available about thermal inactivation of CSFV beyond that gathered by the OIE and EC, but data about other animal viruses confirms the susceptibility of viral agents to inactivation at relatively mild temperatures over short periods of time. Supporting evidence is also present in bacterial studies since viruses are generally easier to inactivate than bacteria.<sup>8</sup> Flash pasteurisation of milk at 71.6° C for 15 seconds successfully inactivates most bacteria.<sup>9</sup>

#### **2-1-4 Desiccation**

In general, viruses do not respond well to physical alterations of the surrounding environment such as drying. According to OIE experts at the Diagnostic Virology Laboratory of the National Veterinary Services Laboratory (US), little information is available on the response of virus to drying.

### **2-2 EAPA Members Process Description (Spray-Drying)**

See **Spray-Drying Process** section on A description of Manufacturing Process of SDAP document.

### **2-3 Analysis of EAPA Members Process (Spray-Drying)**

Either thermal inactivation or inactivation by dehydration have been suggested as mechanisms that may contribute to microbial inactivation during the spray drying process<sup>10,11,12,13</sup>. Both mechanisms occur simultaneously and affect the microorganism differently depending on the microorganism's resistance to heat or dehydration. Some microorganisms adapt to high temperatures. The short drying time with the almost immediate increase in temperature does not allow the microorganism the time to adapt to high temperature<sup>14</sup>. Lievens<sup>15</sup> suggested that the cell damage or mortality caused by thermal inactivation is due to an effect on DNA, RNA, and key proteins. Dehydration leads to the loss or inactivation of cell components including cations, nucleotides, enzymes, proteins and amino acids<sup>16,17,18,19,20</sup>. Zimmermann<sup>21</sup> suggested the rapid removal of water was important in microbial inactivation.

In experiments conducted by EAPA Members, PRV and PRRS virus were added to bovine plasma and subsequently spray dried. Pre-drying PRV titer was  $10^{5.3}$  TCID<sub>50</sub> / ml and no virus was detected post-drying after 4 serial passages. Pre-drying PRRS titer was between  $10^{4.0}$  and  $10^{3.5}$  TCID<sub>50</sub> / ml and could not be detected after 4 serial passages. These data indicate that spray drying inactivated both viruses. Polo et al.<sup>22</sup> reported that spray drying reduced E. coli over 5 log units.

Over the past 20 years random samples of commercially produced spray dried animal plasma have been submitted to Iowa State University Diagnostics Laboratory for viral screening (Bovine reovirus, Infectious Bovine Rhinotracheitis virus, Bovine Para-Influenza type 3 virus, Porcine Parvo Virus, PRRS, Transmissible Gastroenteritis virus, Swine Influenza Virus, Rabies virus, Blue Tongue; Code of Federal Regulations for Ingredients of Animal Origin, 9 CFR, Part 113, 1996). Viral contamination has never been reported (personal communication M. Van den Berg, 2003).

In a seroconversion trial conducted by an EAPA Member, specific pathogen free (SPF) pigs housed in isolated facilities were fed a diet containing 8% spray dried plasma for 62 days. A typical plasma protein effect was observed as indicated by improved daily gain over the period 0 to 42 days ( $P < 0.10$ ). To determine if the pigs were or became infected with PPV, PRV or PRRS blood samples were taken to determine the presence of antibodies at the beginning and throughout the experiment. Antibodies were not detected to any of these viruses indicating that the pigs did not become infected. Clinical signs of disease were not noted in the pigs consuming the plasma containing diet<sup>23</sup>.

According with OIE standard procedure and Council Directive 2002/99/EC that establish the relevant sanitary treatment to inactivated CSF in meat, the heat treatment at a minimum temperature of 70°C which must be reached throughout the meat is enough to inactivated this virus. The spray drying temperature to dehydrated porcine plasma and other blood derivatives have an inlet temperature of 160°C -300°C (minimum contact time is between 10 to 30 seconds) and an outlet temperature of 70-90° C, therefore the product have the requested inactivation temperature through their substance.

Considering the temperature sensitivity of viruses and the circumstantial evidence of thermal inactivation, it is reasonable to conclude that spray-drying reduces significantly the risk of CSFV in the plasma product. Physical factors such as pressure and desiccation may also contribute to virus inactivation. However, ambiguity regarding virus response to changes in the physical environment clearly contributes to uncertainty in the overall assessment, and further research is needed to elucidate the impact of each factor.

## **2-4 Spray-Drying Score: Reduces Significantly the Risk**

# **3 Risk Factor: Bagging**

## **3-1 Issues of Concern (Bagging)**

Contamination of the dried product during the bagging process is unlikely, particularly if access to the bagging room is controlled. Use of a dedicated facility and trained personnel who do not work with the raw product is essential.

### **3-2 EAPA Members Process Description (Bagging)**

See **Overview of the Manufacturing Process**, on “A description of Manufacturing Process of SDAP” document.

### **3-3 Analysis of EAPA Members Process (Bagging)**

Control measures are in place to ensure minimal contamination of the final product. The spray-dried plasma has low moisture content (less than 10%) and contains no preservatives. Bagging in small quantities sealed in plastic and protected from light helps prevent spoilage.

### **3-4 Bagging Score: No Impact on Risk**

## **4 Risk Factor: Quality Assurance**

### **4-1 Issues of Concern (Quality Assurance)**

During processing and packaging at the plant, quality control measures are required, not only to prevent cross-contamination, but also to detect potential contaminants in the final product, and allow for recall of any batch if necessary. Control measures include routine inspection of the processing plants by state regulatory officials. Within the plant, dedicated personnel following standard operating procedures work each step of the process. Processing occur in closed systems as much as possible.

#### **4-1-1 Laboratory Testing**

To monitor product quality with regard to disease transmission, reconstituted dried plasma undergo randomly laboratory testing for known disease agents. If for some reason like a disease outbreak in a specific region occurs laboratory testing could be done for all production batches to assure the absence of the specific pathogen.

#### **4-1-2 Recall**

A recall system that identifies each bag of dried product, its associated plasma batch, and its geographical and customer destination is in place. This means that EAPA Members system are prepared if the Veterinarian Authorities request to hold the material during a certain period or destroyed, irradiated or tested according to official policy.

## **4-2 EAPA Process Description (Quality Assurance)**

EAPA Members are ISO 9001 and/or GMP certified. Most of the plasma processing plants in Europe are food grade approved and is periodically inspected by an official veterinarian from the Public Health Department and an EU official veterinarian.

Prior to entering into the drying chamber all steps occur in closed systems with standard operating procedures for cleaning, maintenance, and use. Movement of the dried plasma from the spray-dryer to a dedicated bagging area is a controlled process. A recall number that identifies the batch of plasma from which it originated is printed on each bag, and the geographical destination of each shipment of bagged plasma is recorded.

## **4-3 Analysis of EAPA Members Process (Quality Assurance)**

Measures to ensure minimal likelihood of cross-contamination during processing and packaging have been established. The plasma processing plants are inspected randomly by official regulatory agents, and an effective recall system is in place should a problem arise.

Similarly, Iowa State University testing yielded negative results for Bovine Viral Diarrhoea (BVD), a virus antigenically related to CSFV. Both belong to the genus *Pestivirus* of the family *Flaviviridae*. BVD is present in cattle throughout the US, particularly in feedlots and dairy herds. Plasma sourced from areas in which BVD is known to exist, harvested at local slaughterhouses and processed through a Blood Producer facilities in US failed to contain BVDV in the final product. Considering the morphological and antigenic similarities between BVDV and CSFV, it is reasonable to assume that factors inactivating the former would similarly effect the latter.

## **4-4 Quality Assurance Score: Reduces Risk**

## 5 Summary of Processing

### 5-1 European Union

Risk considerations and outcomes for the processing section of this assessment

**Table 3: Summary of Risks Associated with Processing – EU**

RISK FACTOR	GRADE	COMMENTS
Post-Harvesting Score	Low	See ' <b>Harvesting</b> '
Concentration	No Impact on Risk	Partially removes cell-associated virus if present, may concentrate other viruses
Spray-Drying	Reduces Significantly the Risk	Physical inactivation
Bagging	No Impact on Risk	Control measures in place
Quality Assurance	Reduces Risk	Confirms virus inactivation through spray-drying. Possibility of irradiation.
Cumulative Score Post-Processing	Remote-Minuscule	

There is a remote-minuscule risk that spray-dried plasma for animal consumption that is sourced from the EU will contain CSF infectivity. The main factors influencing this assessment are the low risk post-harvesting, the physical challenges of spray-drying (primarily heating), the confirmation of virus inactivation by independent sources, and the absence of CSFV in standard product testing during an outbreak of this disease in Spain. Although there is little information regarding the effects of spray-drying on CSFV, extrapolation from experiments on other viruses suggests that exposure to a high temperature over a short period of time results in virus inactivation. Increased pressure and desiccation may also cause significant viral damage.

## d) Product Use - CSF Disease

### 1 Risk Factor: Specie of destination (Swine)

#### 1-1 Issues of Concern (Specie of destination)

CSF affects domestic and wild swine.

Plasma contains antibodies against different micro-organisms, including pathogenic bacteria, viruses and toxins. The antibody content depends on environmental challenges and is species-specific. Therefore, another approach to the species barrier issue would be to examine the benefits of using plasma antibodies as protection against species specific infections, especially as passive immunity protection against local intestinal infections.

#### 2-4 Specie of destination: Potential to Increase Risk.

### 2 Risk Factor: Route of Transmission

#### 2-1 Issues of Concern (Route of Transmission)

Naturally occurring List A disease agents gain entrance into their hosts by a multitude of pathways, including transcutaneously (skin abrasion, arthropod vectors), via the respiratory system (aerosol droplets), or by ingestion. Transmission of CSFV is primarily by direct contact, fomites, and swill feeding.<sup>3</sup>

#### 2-2 EAPA Members Process Description (Route of Transmission)

Spray-dried plasma is intended for use in animal feedstuffs. Therefore ingestion is the major route of exposure; abrasion of the oral mucosa may provide an alternate route of entry. Because of the proximity of the eyes and nose to the feed source exposure through the conjunctiva and respiratory routes are theoretically possible

#### 2-3 Analysis of EAPA Members Process (Route of Transmission)

Considering the relative susceptibility of viral agents to physical and chemical inactivation, few viruses are likely to survive the rigors of the gastrointestinal tract. CSFV is infectious by the oral route, but infection in this manner usually requires very large amounts of the disease agent such as occurs in swill feeding<sup>24,25</sup> when the source is infected and the heat processing inadequate to inactivate the virus.

## **2-4 Route of Transmission Score: Reduces Risk.**

# **3 Risk Factor: Dose**

## **3-1 Issues of Concern (Dose)**

As with most infectious diseases, a susceptible animal must receive a sufficient dose of the infectious agent if disease is to result. Assuming that CSFV is present in the final product, the dose delivered to an animal would depend on the initial infectivity, the inclusion rate of spray-dried plasma in the feed, and the probability of encountering the agent as a function of time over which plasma products are ingested.

### **3-1-1 Infectivity**

Infectivity is an inherent property of a disease agent. Some pathogens retain infectivity throughout most of their lifecycle, while others must undergo structural or chemical alteration before becoming infective. Several viruses transmitted by arthropod vectors fall into the latter category in that replication and multiplication within an arthropod or other host is an important phase of their lifecycle.<sup>8</sup> Replication within an arthropod magnifies the infectious dose delivered to the next susceptible host.

CSFV retain infectivity without the necessity of additional multiplication/replication or other alteration.

### **3-1-2 Inclusion Rate**

Assuming that infective CSFV is present in the final product, the risk of encountering either agent in sufficient quantity to cause disease increases with greater inclusion rates of dried plasma in the feed.

### **3-1-3 Length of Feeding**

Assuming CSF infectivity exists in the final product, the risk of encountering a batch containing an infectious agent increases as the time period of consumption lengthens. This is based on probability, since there is little evidence for an additive effect of long-term exposure to any of these viruses.

### 3-2 EAPA Members Process Description (Dose)

Porcine Spray-dried plasma is gaining recognition as a valuable addition to piglet: current research indicates that plasma in the diet increases weight gain during this crucial period, and may protect the gastrointestinal system.<sup>26,27,28,29</sup> The inclusion rate in piglet weaning diets is around 2-10% (average 5%) and piglets usually remain on the diet for 7-14 days post-weaning.

### 3-3 Analysis of EAPA Members Process (Dose)

As mentioned above, ingestion is a natural route of infection for CSFV, although infection by oral route requires very large amounts of the virus. Concentration of infective virus usually only occurs if swine are fed untreated swill.<sup>3,25</sup> It is therefore unlikely that a susceptible piglet would receive an infectious dose of CSFV at the current inclusion rates.

In addition, sequential pooling of blood and plasma, as occurs in the harvesting and processing steps of spray-dried plasma production, results in dilution of potentially infectious agents and thereby reduces risk of any one animal receiving an infectious dose

### 3-4 Dose Score: Reduces Risk

## 4 Summary of Product Use

**Table 4: Summary of Risks Associated with Product Use - European Union**

RISK FACTOR	GRADE	COMMENTS
Post-Processing Score	Remote-Minuscule	See ' <b>Processing</b> '
Specie of destination	Potential to Increase Risk	
Route of Transmission	Reduce Risk	Stomach barrier
Dose	Reduces Risk	Small amounts of plasma product fed over a short period of time
Cumulative Score Post-Use	Minuscule	

There is a Minuscule risk that spray-dried plasma products processed from blood collected in the EU will contain OIE List A infectivity and transmit such diseases when used in the intended manner. The main factors influencing

this assessment are the remote-minuscule risk associated with the dried plasma post-processing, the ineffectiveness of ingestion as a route of transmission, and the minimal likelihood of livestock receiving an infectious dose should CSF.

## **e) Risk Management and Risk Communication**

EAPA Members computerised Quality Control Data Base, keeps the following information:

- production lot number, that identifies manufacturing plant, date of production, production line, expiry date and production shift
- physico-chemical and microbiological analysis for every production lot
- physical situation of the lot (warehouse, quarantine, availability for sale)
- destination of the product (customer, lot number, date of delivery, quantity)

This information allows EAPA Members to trace any lot number from the source of incoming blood (collection site and farm) to the destination of the final product (customer) in hours. In the hypothetical situation of a potential hazard this permits EAPA Members to react immediately, immobilising the product in their facilities, and informing the customer if the product has already been delivered.

EAPA Members maintains collaboration agreements with universities, research centres and official analysis laboratories to contrast the analytical methods used, and check for the absence of different viruses and pathogenic micro-organisms externally, either for random analysis and in special cases.

Direct contact with Authorities, agreements with universities and specialised consultants ensure that EAPA Members is constantly informed of changes in legislation or any new requirements.

The close contact with official veterinarians and health authorities keeps EAPA Members informed about potential new hazards and measures to implement.

## f) Additional Tables

**Table I: Specific OIE List A Diseases: General Information and Inactivation Data<sup>6</sup>**

DISEASES	CAUSATIVE AGENT	TEMPERATURE INACTIVATION	pH INACTIVATION	TRANSMISSION	HOSTS OF INTEREST	OTHER HOSTS
Classical Swine Fever	Pestivirus, family <i>Flaviviridae</i>	70°C throughout their substance	Stable pH 3-11	Contact, fomites, food waste, transplacental	Swine only	Wild boar

## g) Summary Tables for EU Region

**Table II: Summary of Risk Assessment for CSF Disease in the European Union**

RISK FACTOR	GRADE	COMMENTS
Country of Origin	Low	Control strategies at country and EU level limit BT, CSF and SVD
Herd of Origin	Potential to Reduce Risk	Geographical distance may limit risk
Individual Source Animal	No Impact on Risk	
Disease Characteristics	Potential to Increase Risk	Existence of sub-clinical or incubating cases increases risk if disease present
Tissue Type	Increases Risk	BTV, CSFV and SVDV are present in the blood of affected animals
Harvesting: General Considerations	Decreases Risk	<i>Ante mortem</i> inspection removes clinically affected animals
Tissue Collection	Potential to Increase Risk	Pooling blood may increase risk
Post-Collection Handling	Potential to Increase Risk	Pooling plasma may increase risk
Concentration	No Impact on Risk	Partially removes cell-associated virus if present, may concentrate other viruses
Spray-Drying	Reduces Significantly the Risk	Physical inactivation
Bagging	No Impact on Risk	Control measures in place
Quality Assurance	Reduces Risk	Confirms virus inactivation through spray-drying
Specie of destination	Potential to Increase Risk	
Route of Transmission	Reduce Risk	Stomach barrier
Dose	Reduces Risk	Small amounts of plasma product fed over a short period of time
<b>CUMULATIVE SCORE</b>	Minuscule	

### 3 Final Conclusions

There is a minuscule risk that porcine spray-dried plasma for animal consumption that is sourced from EU will contain CSF infectivity. The main factors influencing this assessment are the remote risk post-harvesting, the physical challenges of spray-drying (primarily heating), the confirmation of virus inactivation by independent sources, and the absence of viruses in standard product testing. Increased pressure and desiccation may also cause significant viral damage.

With respect to CSF disease in the EU, systematic rejection of blood from carcasses condemned on *post mortem* examination has a reduction impact on the risk of disease transmission through spray-dried plasma intended for animal consumption.

This study aims to have made a contribution to the knowledge of manufacturing processes, products and applications of spray-dried blood derivatives for animal nutrition.

It is believed that the results of the internal studies carried out by EAPA Members can justify the claims made for the safety of the described products and processes, thus maintain and increasing confidence in their use. Spray-dried blood derivatives are safe, functional and highly nutritional ingredients.

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