



*Groupement Européen des Produits Oléochimiques
& Associés*

A Sector Group of CEFIC

*The European Oleochemicals & Allied
Products Group*

Avenue E. Van Nieuwenhuysse 4, bte 1

B – 1160 Brussels

Tel. : 32 2 676 7211

Fax: 32 2 676 7301

<http://www.apag.org>

THE SAFETY OF TALLOW DERIVATIVES WITH RESPECT TO BOVINE SPONGIFORM ENCEPHALOPATHY

AN UPDATED REPORT – AUGUST 2003

EXECUTIVE SUMMARY

Tallow derivatives produced by members of the European Oleochemicals and Allied Products Group (APAG) are used extensively in food, animal feed, cosmetics, medicinal and pharmaceutical products and a wide range of industrial applications. This report provides support for the safety of tallow derivatives with respect to bovine spongiform encephalopathy and updates the papers prepared by APAG in February 1996 which was revised in May 1997, in May 1998, in March 1999 and lastly in March 2002. In these reports, the safety of tallow derivatives is based on the rigorous processes applied by the oleochemical industry.

In a scientific opinion published in March 1998, the EU Scientific Steering Committee (SSC) considers tallow derivatives to be safe providing:

- the raw material for tallow production is fit for human or animal consumption, or,
- regardless of the source of the material, and regardless of the type of material, the production process uses the appropriate, validated and scientifically most up-to-date methods in terms of inactivating the BSE agent. Several amongst them have been listed in the scientific opinion of the Scientific Committee on Cosmetology and in the opinion of the Committee of Proprietary Medicinal Products.

Consequently, from this opinion it would follow that manufacturers complying with the listed validated inactivation methods could process tallow to tallow derivatives regardless of its source and regardless of the type of material used in its production and that such tallow derivatives could be regarded as safe to use for any purpose.

However, depending of the intended end use, the SSC also recommends that the raw material for tallow production should be obtained from appropriate sources (geographical, animal), animal species and tissues. Where required, appropriate rendering conditions should be used. In addition, the SSC strongly recommends the introduction of HACCP in the manufacture of tallow, in particular w.r.t. traceability and treatment at origin of the raw material.

Most Decisions, Regulations and Directives adopted or proposed by the Commission in the last two years reflect these opinions and in certain cases go beyond these. They concentrate around three basic principles: origin of material and processes for tallow manufacture (countries, parts of the animal, rendering conditions), quality control measures and processing conditions of tallow derivatives.

The current report updates the previous one to take this legal framework into account and addresses:

- the various conclusions from the Scientific Steering Committee on the safety of tallow and processes for the manufacture of tallow derivatives w.r.t. BSE
- inactivation studies with tallow
- the relevant legislation proposed and currently in force. Repealed legislation has not been taken up in this report anymore
- the production of tallow
- the processing of tallow to produce fatty acids, glycerol and other derivatives (fatty alcohols, metallic soaps, fatty amines, fatty amides, fatty acid esters)
- The principles of Hazard Analysis Critical Control Points (HACCP)



The conclusion is reached that with the current scientific opinions, the legislative provisions in place and the processes applied by the oleochemical industry, tallow derivatives can be considered to provide the highest degree of safety with regard to BSE for use in human food, animal feed, pharmaceuticals and cosmetics.

To further support this conclusion, APAG is in the process of validating the process conditions considered to be safe by the SSC in its scientific opinion of March 1998. These validation studies will include the hydrogenation and the hydrolysis of animal fats. The latter process amongst others under conditions referred to in a number of current legislative provisions (200°C at corresponding pressure for 20 minutes) to show that the resulting fatty acids and glycerine are free of BSE infectivity.



THE SAFETY OF TALLOW DERIVATIVES WITH RESPECT TO SPONGIFORM ENCEPHALOPATHY
AN UPDATED REPORT - AUGUST 2003

Contents

| | |
|--|---------|
| 1. Introduction | page 4 |
| 2. The Safety of tallow and tallow derivatives | page 4 |
| 2.1. Scientific opinions on the safety of tallow and tallow derivatives | |
| 2.2. Opinions of other bodies on the safety of tallow and tallow derivatives | page 8 |
| 2.3. Safety studies with tallow | page 9 |
| 3. Directives, Regulations and Decisions | page10 |
| 3.1. On tallow | page 10 |
| 3.2. Cosmetic products | page 10 |
| 3.3. Pharmaceutical products | page 10 |
| 3.4. Food, animal feed, fertilizers | page 11 |
| 3.5. United Kingdom and Portugal | page 11 |
| 4. Tallow | page 12 |
| 4.1. Background | page 12 |
| 4.2. Production of tallow | page 12 |
| 5. Production of tallow derivatives | page12 |
| 5.1. General | page 12 |
| 5.2. Fatty Acids | page 12 |
| 5.3. Fatty Alcohols | page 13 |
| 5.4. Glycerol | page 14 |
| 6. Hazard Analysis of Critical Control Points | page 15 |
| 7. Conclusions | page 16 |
| 8. References | page 17 |
| Annex I: Flowsheet for the manufacture of esters from rendered fats | page 18 |
| Annex II: Flowsheet for the manufacture of fatty alcohols from rendered fats | page 19 |
| Annex III: Flowsheet for the manufacture of glycerine from rendered fats | page 20 |



1. INTRODUCTION

Tallow is an important raw material for the oleochemical industry and is used in the production of tallow derivatives (fatty acids, fatty alcohols, metallic soaps, fatty amines, fatty amides, fatty acid esters, and glycerol) for use in foods, animal feed, pharmaceutical and cosmetic products and a wide range of industrial applications. These derivatives are produced from tallow by a variety of aggressive physico-chemical processes involving high temperature and/or high alkalinity and purification (e.g. distillation or ion exchange). In many cases they are subject to further down stream chemical transformations.

Tallow is primarily extracted from the tissues of bovine, ovine, and caprine origin. Because of public health concerns relating to Bovine Spongiform Encephalopathy (BSE) and other Transmissible Encephalopathies (TSE) from animal derived materials there is a need to give assurance that tallow derivatives are considered safe for use in food, feed, medicinal, pharmaceutical and cosmetic products and indeed in industrial products.

APAG published a first report in February 1996, which assembled all the evidence available at the time to provide this assurance. The report was circulated for consideration by the Commission, by the EU Committee on Proprietary Medicinal Products and by the International Pharmaceutical Excipients Council (Europe). The report was updated in May 1997, in May 1998, in March 1999, March 2002 and lastly in November 2002

The current report is an update of the November 2002 report to take into consideration:

- the various conclusions from the Scientific Steering Committee on the safety of tallow and tallow derivatives w.r.t. BSE
- the relevant legislation proposed and currently in place
- the production and safety of the tallow used by the oleochemical industry
- the processing of tallow to produce fatty acids, glycerol and other derivatives (fatty alcohols, metallic soaps, fatty amines, fatty amides, fatty acid esters)

2. THE SAFETY OF TALLOW AND TALLOW DERIVATIVES.

2.1 Scientific opinions on the safety of tallow and tallow derivatives.

In March 1998 (ref.1) the Scientific Steering Committee (SSC) of the European Union published a scientific opinion on the safety of tallow derived from ruminant tissues w.r.t. BSE in which the following question was raised:

“Can tallow be considered to be free of BSE infectivity, regardless of the source of the material (geographical and animal), regardless of the type of material used for its manufacture (such as Specified Risk Material), regardless of the age of the animal and regardless of the production process, but provided it is free from proteinacious material as a result of appropriate purification”.

From the wording of this question it can be concluded that the SSC considers three basic principles relevant to the safety of tallow: origin of material for tallow manufacture (countries, parts of the animal), processing (rendering conditions, purification) and processing conditions of tallow derivatives.

For the purpose of the opinion, tallow was defined as fats obtained by pressing or any extraction system down from ruminant tissues which are derived directly from adipose tissue, from fat extracted from skeleton muscles, from mechanically recovered meat and from rendered animal waste including bones. Appropriate purified tallow was defined as tallow with maximum levels of remaining total insoluble impurities of 0.10 – 0.15 %.

The SSC expressed as its opinion that tallow, appropriately purified, is in principle safe. However, depending of the intended end use, the raw material for tallow production should be obtained from appropriate sources (geographical, animal), animal species and tissues. Where required, appropriate production processes should be used. The SSC also strongly recommended the introduction of HACCP in the manufacture of tallow, in particular w.r.t. traceability and treatment at origin of the raw material.



For critical end uses such as human food and animal feed the SSC more specifically recommended that tallow derived from animals fit for human consumption should be used which needs to be appropriately purified if sourced from countries or regions with no or negligible BSE risk. If sourced from a region or country with low BSE risk in addition no SRM should be used and if sourced from a high risk region or country tallow should, on top of appropriate purification and SRM removal, have been processed at 133 °C at 3 Bar for at least 20 minutes. Tallow not fit for human consumption could be used for animal feed only provided it is purified appropriately and is sourced from countries with no or negligible BSE risk and further provided that tallow has been processed at 133 °C at 3 Bar for at least 20 minutes and is not derived from SRM.

For industrial end use (not tallow derivatives), the SSC recommends that tallow be appropriately purified if derived from animals fit for human consumption and if derived from animals not fit for human consumption is appropriately purified and rendered at 133 °C at 3 Bar for at least 20 minutes.

The SSC also raised the question of safety of tallow derivatives and concluded:

“Tallow derivatives can be considered to be safe, providing

- a) the raw material is fit for human consumption, or regardless of the source and type of the material*
- b) the production processes uses the appropriate methods to inactivate TSE agents.*

These methods have been defined by the Committee for Proprietary Medicinal Products (CPMP) and the European Agency for the Evaluation of Medicinal Products (EMA).”

This would imply that neither appropriate purification, nor specified rendering conditions, nor SRM removal is necessary for tallow derivatives obtained from tallow processed under the above certified conditions.

On 24-25 June 1999 (ref.2), the Scientific Steering Committee of the EU adopted a scientific opinion on the “risks of non conventional transmissible agents (BSE), conventional infectious agents or other hazards such as toxic substances entering the human food or animal feed chains via raw material from fallen stock and dead animals or via condemned animals”. The conclusions were as follows:

- a) The rendering standard of 133 °C/20minutes/3 Bar is not completely safe for clearing TSE infectivity in tallow, if the initial infection is high. Therefore the recycling or disposal of condemned animals and materials should not lead to human and animal consumption or use in cosmetics and pharmaceuticals.
- b) The standard rendering conditions are appropriate for conventional infectious agents
- c) If the cause of death or the reason for animals to be condemned do not constitute a direct or indirect risk for human or animal health or for the environment, the material may be considered as being of no or low risk. Processing into products for animal consumption, industrial use or use as fertilizer is acceptable. The standard rendering conditions must be applied.
- d) If the cause of death or the reasons for animals to be condemned cannot be identified, or if appropriate rendering conditions do not exist, they should be disposed of in such a way that any further processing into products for human or animal consumption is excluded. The SSC considers all material from dead animals in principle as condemned.
- e) Animals and materials that carry a potential, suspected or actual TSE risk should be disposed of, incinerated or burned after previous rendering at the standard conditions.
- f) Recycling of SRM’s is only acceptable for certain industrial/technical uses.

The basic reasoning in the above is that the risk from dead animals and condemned materials depends (i) on the origin of the material, (ii) the reason why the animal died or was killed, (iii) whether or not the cause or reason can reliably be determined, (iv) whether or not recycling processes are available capable of mitigating the risk and (v) on the end/final destination of the recycled products.

The SSC again confirmed that:

“Tallow derivatives which do not contain proteins or peptides are safe, providing the raw material is fit for human consumption or, regardless of the source and type of the material, the production processes uses the appropriate methods to inactivate TSE agents.”



On January 12, 2001 (ref.3) the Scientific Steering Committee again reviewed the use of rendered fats in animal feed. It was concluded that any tallow for animal feed purpose obtained from a country with more than a negligible BSE risk must have been rendered at 133 °C at 3 Bar for at least 20 minutes and be appropriately purified. This is a more severe requirement than expressed in the March 1998 opinion where such treatment was only required for countries with a high BSE risk (see above).

In June 2001 (ref.4) the SSC revised its opinion on the safety of tallow w.r.t. TSE, replacing its earlier opinions cited above. As a general principle the SSC concluded that:

1. There is no evidence that tallow derived from ruminants presents a TSE risk. Possible TSE risks can only result from protein impurities
2. The safety of tallow must be assessed by applying three criteria: sourcing of animals and tissues (geographical, animals fit or not fit for human consumption, SRM), fat extraction processes (residual proteinaceous material) and sterilisation processes (such as 133°C, 20 min., 3 Bar).
3. In all cases, sourcing from animals healthy at the time of slaughter will reduce TSE risks. For countries with suspected or proven TSE (GBR II, III and IV) removal of SRM will further reduce TSE risks.
4. Given the fact that animals and materials that carry an actual or suspected TSE risk (SRM) should be disposed of, purified tallow derivatives can be considered to be safe if manufactured under validated process conditions. The material for tallow manufacture must be sourced according to the SSC opinion of June 1999 on fallen stock and condemned materials (SRM).
5. Strict separation of storage, transport and use of tallow is needed to avoid cross-contamination.

Following the above principles, the SSC recommended for tallow obtained from animals fit for human consumption:

1. Tallow obtained from melting discrete fat tissues intended for human consumption that was handled as such is as safe as meat and can be used in all applications including food, animal feed, cosmetics and pharmaceuticals. Tallow from other discrete adipose tissues not intended for human consumption is also safe for use in all applications with the exception of food. In countries with a GBR classification other than I, SRM must be removed.
2. The SSC notes that purification of tallow to < 0.02% insoluble material as currently practiced by European fat melters further reduces TSE risks.
3. Tallow obtained from the rendering of other tissues can be safely used for all applications including food if originating from a country with GBR classification I. For all other countries use in animal feed (except calves) and in the manufacture of tallow derivatives is allowed provided SRM has been removed, tallow has been purified to levels below 0.15% insoluble materials and a pre-sterilisation process has been applied. So far only a pre-sterilisation of fresh tissues at 133°C for 20 minutes at 3 Bar has been evaluated and found to be effective.
4. As no results are available on the safety of post-sterilisation of tallow, tallow originating from other countries than GBR I, from tissues other than adipose tissue not obtained with pre-sterilisation, can only be used for certain industrial applications and for the manufacture of tallow derivatives.

For tallow obtained from animals not fit for human consumption, the SSC recommends:

1. Tallow originating from animals not fit for human consumption can be used for industrial applications (i.e. not food, animal feed, cosmetics and pharmaceuticals) and for the manufacture of tallow derivatives, provided SRM has been removed and it has been purified to contain < 0.15% insolubles.

On 29 – 30 November 2001 (ref.5), the Scientific Steering Committee adopted an opinion on the hypothesis on the origin and transmission of BSE. This opinion in essence reviews all existing information on the agent responsible for BSE and the origin and transmission of BSE.



Conclusions relevant to the oleochemical industry are:

- the origin of BSE is not known
- the agent responsible for BSE is believed to be a prion protein
- Meat and Bone Meal (MBM) is the most important vehicle for transmitting BSE
- A range of ruminant tissues show BSE infectivity (SRM)
- Infectivity in tallow has not been found
- Tallow derivatives are most unlikely a source of BSE given the rigorous processes applied.

The Scientific Steering Committee circulated on February 28, 2002 a draft document on residual TSE risks in gelatine and tallow derived from bones (bone fat). Following a risk assessment procedure adopted by the SSC in 2000 the following observations were made w.r.t. tallow:

1. Although the worst case scenario would be one in which all of the infectivity in the raw materials ends up in the tallow after processing, such a scenario has not been considered in the risk assessment since there is sufficient evidence that this does not occur in practice. Experimental studies have shown that BSE and scrapie infectivity tend to partition preferentially with meat and bone meal and not with tallow (Taylor). Tallow produced under worst case conditions (unfiltered) had no detectable infectivity.
2. Although BSE infectivity goes with meat and bone meal, it must be recognised that there are insoluble impurities, including proteins, which adventitiously end up in tallow during the extraction (rendering) process. Since BSE infectivity fractionates with the proteinaceous rather than the fatty fraction, the effect of protein contamination must be separately evaluated.
3. The level of insoluble impurities in tallow decanted from large holding tanks can be as high as 0.5%. The proportion of proteins in these insoluble solids is unknown, but can be potentially high. However, tallow at the end of the extraction process is purified to a maximum solid content of 0.15% as recommended by the SSC in March 1998. It is estimated that around 85% of this are proteinaceous impurities.
4. Following the various scenario's, the residual TSE risks in tallow derived from bones is extremely low and could be caused only by adventitious contamination.

In April 2003 (ref.6), the SSC adopted a final opinion specifically on the safety of tallow derivatives:

“ Given the pharmaceutical, cosmetic and food applications of tallow derivatives, the SSC considers it is justified to modulate the risk reduction according to the source of the tallow used for the production of the derivatives and the geographical BSE risk level:

a) Tallow derivatives are safe with regard to BSE risk regardless of the production process if they are derived from food- or feed- grade tallow and if cross contamination is prevented. The criteria for food- and feed-grade tallow are detailed in the SSC opinion of 28-29 June 2001 on the safety of tallow obtained from ruminant slaughter by-products.

b) Tallow derivatives are safe with regard to BSE risk regardless of the production process if they are derived cattle from GBR-C I countries and fallen stock are excluded.

c) For GBR-C II countries, tallow derivatives are safe if fallen stock are excluded, the animals from which the tallow is sourced are fit for human consumption, the raw tallow is produced according to the standards indicated in the SSC opinion of 28-29 June 2001 on the safety of tallow (including filtration), the processing conditions described in the mandate have been used and cross contamination is prevented.

d) For GBR-C III and IV countries, tallow derivatives are safe if, in addition to the above (c), the specified risk materials have been removed and are not used for the production of tallow / tallow derivatives.



It is to be noted that feed grade tallow is now known as tallow from Category 3 animal by-Products tallow as defined in the Animal By-Products Regulation 2002/1774/EC. The main difference with the previous opinion is that removal of SRM is not necessary if the derivatives have been produced from tallow originating from animals fit for human consumption in countries with GBR II status.

In June 2003, the SSC adopted a document on the GBR status of many countries. This document also gives a summary opinion on the efficiency of the standard rendering conditions to inactivate the BSE agent:

A rendering process is regarded to be able to significantly reduce BSE-infectivity if it complies with the "standard" of sterilization under temperature/pressure of 133°C/3bar for at least 20 minutes "batch pressure cooking". The pressure refers to the pressure of steam in the airless cooker and the material has to have a maximum size of 5 cm and a moisture content of about 60% when entering the cooker. These conditions are referred to by "the 133°C/20min/3bar standard".

- If all rendering plants that process ruminant materials reliably operate the 133°C/20 min/3bar standard, the SSC assumes, for all practical purposes, any infectivity would be reduced by a factor of at least 1000. Under this condition rendering is considered as "OK".

- If only rendering plants that process "high risk" material (i.e. fallen stock, condemned materials and animals condemned in ante mortem inspection) reliably operate the standard, rendering is considered as "reasonably OK".

- If high and low risk material is rendered under sub-standard conditions, or if the evidence provided for the reliable application of the standard conditions is insufficient, rendering is considered as "not OK", even if individual rendering plants might comply with the standard.

2.2 Opinion of other scientific bodies on the safety of tallow and tallow derivatives.

In May 1995, the World Health Organisation (Ref.7), in its report WHO/CDS/VP/95.145 notes that "Because of the proteinaceous nature of the TSE agents they would tend to remain with the cellular residues of meat and bone meal during the extraction process, rather than be extracted with the lipids of tallow. For these reasons tallow does not appear to be a risk for human and animal health"

In 1992 the EC Committee on Proprietary Medicinal Products (CPMP) (Ref.8) issued guidelines on the Quality, Safety and Efficacy of medicinal products for human and animal use. Addendum 2 of these guidelines dealt with "Minimising the risk of transmitting agents causing Spongiform Encephalopathy via Medicinal Products". The Guidelines make the following statement relevant to tallow and tallow derivatives: "Materials derived from rendered carcasses and subjected to rigorous processes of extraction and purification (for example triglycerides, glycerol and sorbitan esters, etc. manufactured from tallow) may be considered unlikely to be contaminated. These process conditions far exceed the generally recognised minimum inactivation conditions of 133°C, 3 bar for 20 minutes, or 20°C, with 1 Molar NaOH for one hour.

This position was reiterated by the CPMP Biotechnology Working Party in their meeting on 7-8 May 1996. Also at the CPMP's 26th Plenary Meeting on 15-16th April 1997, the CPMP confirmed that it remains satisfied with the safety of tallow derivatives. The Committees members also calculated what the potential worst case risk of contracting BSE was from one ampoule of vaccine made with bovine materials assuming that all the cattle had BSE. The answer was 1 in 1,000,000,000,000.

In February 2001 (ref.9), the EU Committee on Proprietary Medicinal Products issued a report "Note for guidance on minimising the risks of transmitting TSE agents via human and veterinary medicinal products". This note updates earlier opinions and concludes again that tallow derivatives are safe provided the following process conditions are applied:



- 1) Transesterification or hydrolysis at not less than 200°C for not less than 20 minutes under pressure (glycerol, fatty acids and fatty ester production); or
- 2) Saponification with NaOH 12M (glycerol and soap) in a batch process at not less than 95°C for not less than three hours; or in a continuous process at not less than 140°C, 2 bars for not less than eight minutes, or equivalent

The Scientific Committee on Cosmetology concluded on 24th June 1997 (ref.10) that tallow derivatives originating from material not fit for human consumption are safe for use as cosmetic ingredients, provided the following process conditions are applied:

- 1) Transesterification or hydrolysis at not less than 200°C for not less than 20 minutes under pressure (glycerol, fatty acids and fatty ester production); or
- 2) Saponification with NaOH 12M (glycerol and soap) in a batch process at not less than 95°C for not less than three hours; or in a continuous process at not less than 140°C, 2 bars for not less than eight minutes, or equivalent

On December 6, 2002 (ref.11), the Scientific Committee on Cosmetic and Non-Food Products Intended For Consumers (SSCNF) revised its opinion on the safety of tallow derivatives for use as a cosmetic ingredient to bring it in line with the opinion of the SSC. The SCCNPF concluded that:

1. the exceptions made for tallow derivatives in its latest opinion concerning the amendment to entry n° 419 of Annex II to Directive 76/768/EEC on cosmetic products (see the Annex of Regulation 2001/3/EC below) are no longer scientifically consistent with the above mentioned scientific opinions of the SSC.
2. Consequently, the SCCNFP recommends that the list referred to in Regulation 2001/999/EC should be supplemented by the ingredients derived therefrom and that no exceptions should be made regarding tallow derivatives.

This revised opinion means that tallow derivatives for use in cosmetic products should no longer be produced from any tallow provided certain process conditions are used, but instead should not be derived from SRM. This has so far not been incorporated in cosmetic specific legislation. It is however required by the Animal By-Products Regulation which takes precedence over older cosmetic Regulations dealing with BSE/TSE's.

2.3 Safety studies with tallow.

In a study carried out by Taylor et al it was demonstrated that rendering conditions are sufficient to inactivate any residual protein in the tallow as evidenced by scientific tests using highly infective starting materials (i.e. SRMs from cattle known to have BSE) (Ref.12).

Research on the ability of commercial rendering processes to inactivate both the BSE and scrapie agents was commissioned by the European Commission DGVI and the British Ministry for Agriculture, Fisheries and Food. The research was carried out at the Institute for Animal Health, Neuropathogenesis Unit in Edinburgh, Scotland and has demonstrated that tallow processed under conditions typical of those used by the rendering industry is free from detectable infectivity.

Animal tissues spiked with known highly infective brain material from BSE and then scrapie infected animals were rendered under experimental conditions designed to imitate those typically used in normal commercial practice across Europe and indeed the world. The protein and tallow produced in this way was injected into the brains of mice. The tallow samples were tested filtered and unfiltered according to normal commercial practice. The tested samples failed to transmit any sign of infectivity to mice, even from systems operating at the lowest time/temperature combinations. Tallow was found to be free from detectable infectivity even when the protein from the same batch transmitted disease to 100% of the mice.



Phase 1 of the rendering inactivation study (BSE) was completed in 1994. The results of the study were enacted by the Commission Decision 94/382/EC of 27th June 1994, which defines the acceptable rendering processes in terms of time and temperature, although the study was not published in the Veterinary Record until December 1995. The preliminary results of phase II of the study (scrapie) were made available to the Scientific Veterinary Committee in February 1996. On the basis of the inactivation data from the BSE and scrapie studies Commission Decision 96/449/EC was published on 18th June 1996. This decision repeals 94/382/EC and establishes the rendering processes permitted for the manufacture of mammalian animal protein intended for use in animal feeds as a minimum of 133 °C, at least 3 bar, for at least 20 minutes. Official publication of the second phase of the study (scrapie) was in summer 1997.

Because the study confirmed no detectable infectivity in the tallow samples tested, both Decision 94/382/EC and Decision 96/449/EC specifically excluded at that time rendered fats from the above processing requirements.

As a result of phase I of the scientific study, epidemiological studies in the United Kingdom and Switzerland, and other risk assessment data, the expert opinion of the WHO (3 & 15 th April 1996) is that *tallow is considered safe if effective rendering processes are in place* (Ref.13).

Prof.Dr. D.Riesner of the University of Düsseldorf studied the inactivation of prions in bone fat, a bone fat water mixture and in pure water at various temperatures. The study demonstrates that prions are inactivated in pure water, are partly inactivated in bone fat at temperatures commonly applied by the rendering industry and are almost completely inactivated in a water 6:1 fat mixture at 170 °C. By extrapolation it is concluded that prions are completely inactivated in said water fat mixture at temperatures above 200 °C. An important observation of the study is that the presence of lipids increases the stability of prions. The protective effect of lipids is explained by hydrophobic interactions protecting prions from hydrolytic attack by water.

DIRECTIVES, REGULATIONS AND DECISIONS RELEVANT TO THE PROCESSING AND USE OF TALLOW AND TALLOW DERIVATIVES

3.1 On tallow

Regulation 2002/1774/EC on animal by-products not intended for human consumption lays down the health rules concerning animal by-products not intended for human consumption. Main Objective of this Regulation is the exclusion of dead animals and condemned material from the feed chain. It simplifies existing EU legislation by creating a consolidated legislative act dealing with all animal by-products not intended for human consumption. Creates three animal by-product categories. Category 1 (a.o. Specified Risk Material as defined by TSE Regulation 2001/999/EC and its amendment Regulation 2001/1326/EC) must be destroyed. Category 2 tallow (a.o. from parts of animals unfit for human consumption) can be processed into fat derivatives for use in organic fertilizers or for other industrial use if processed under minimum process conditions (hydrolysis, saponification) in a category 2 oleochemical plant. Category 3 tallow (from animals fit for human consumption) can be used for all technical applications (including cosmetic and pharmaceutical applications) and animal feed provided it is free from insoluble impurities (< 0.15%). Oleochemical plants can either process category 2 or category 3 tallow and must be approved and registered.

Imports of SRMs and products derived therefrom in the Community is prohibited.

Imports of rendered fats in the EU may be authorised if imported from authorised third countries and further provided that it be processed under minimum conditions for technical use only. Import of rendered fat for use in animal feed must come from approved registered rendering plants and be “free” from insoluble impurities (< 0.15%).

Imported rendered fat derivatives must meet the same requirements as those produced in the EC. A definition of rendered fat derivatives is not given, but will possibly be addressed in an separate Decision.

Following Decision 2003/326/EC amending the animal by-products Regulation 2001/1774/EC, oleochemical plants may continue to process tallow derived from Category 2 or 3 animal by-products in one plant until 31st October 2005, provided that separation of product streams is assured.



3.2 BSE/TSE legislation addressing cosmetic products.

Directive 98/16/EC allows the use of tallow derivatives from tallow not obtained from material free from Specified Risk Material in cosmetic products provided such tallow has been hydrolysed above 200 °C for at least 20 minutes at 40 Bar pressure or saponified with NaOH of at least 12 Molar. Allows the use of tallow derivatives from SRM free tallow without specific processing conditions. Amended by Directive 2000/6/EC correcting the 40 Bar pressure to “at corresponding pressure”.

Directive 2000/6/EC adapting for the 24th time to technical progress Annex II, III, VI and VII of Directive 76/768/EEC confirms that tallow derivatives not obtained from SRM free material can be used in cosmetic products provided such tallow has been hydrolysed above 200 °C for at least 20 minutes at corresponding pressure or saponified with NaOH of at least 12 Molar.

Directive 2003/1/EC adapting to technical progress Annex II to Directive 76/768/EC amends the definition of SRM's in the Annex of Directive 98/16/EC to bring it in line with Regulation 2001/999/EC and its subsequent amendments. See also Regulation 2002/1774/EC on animal by-products.

3.3 BSE/TSE legislation addressing pharmaceutical products.

Directive 1999/82/EC Requires that medicinal products are manufactured by March 2001 in accordance with the Note for Guidance on Minimising the Risk of Transmitting BSE/TSE drafted by the Committee for Proprietary Medicinal Products (CPMP). Tallow derivatives are believed to present minimal risks regarding the transmission of BSE/TSE provided these are manufactured under certified process conditions, i.e. hydrolysed above 200 °C for at least 20 minutes at corresponding pressure or saponified with NaOH of at least 12 Molar. Other process conditions must be at least as robust and rigorous and must be validated. See also Regulation 2002/1774/EC on animal by-products

3.4. BSE/TSE legislation addressing human food, animal feed and fertilizers.

Decision 2001/9/EC: requires the testing for BSE of certain categories of bovine animals over 30 month of age slaughtered for human consumption.

Decision 2001/25/EC prohibits the use of animal by-products derived from fallen stock and other condemned material for the manufacture of feed for farmed animals (animals kept for food production). This prohibition also applies to imports.

Regulation 2001/999/EC on the adoption of a Regulation for the prevention and control of certain TSE's requires that Member States and third countries submit an application to the Commission for their BSE status to be determined. In total 5 categories are introduced. SRM shall be removed and disposed of. The extend to which SRM has to be removed depends on the BSE status.

In Member States placed in Category 5, the feeding to ruminants of rendered ruminant fat is prohibited. EC countries placed in Category 5 are not allowed to produce rendered fats (for food and feed use) from ruminant material, unless it was produced from discrete adipose tissue (body fat) or the raw material for the rendered fat was processed in accordance with the standards referred to in Directive 90/667/EEC, or if ruminants have undergone a BSE test where the result of the test was negative.

When importing a product of animal origin from a non-EC Member country which is not placed in category 1, a declaration must be provided, signed by a competent authority of the country of production, confirming that the product does not contain and is not derived from Specified Risk Material. Products of animal origin imported from a non-EC Member country placed in category 2 – 5 must come from healthy animals. The placing on the EC market of rendered ruminant fat and its derivatives



originating from EC Member countries or from non-EC Member countries or regions placed in category 5 is prohibited unless derived from animals in herds with a certified freedom of BSE for at least seven years or the animals were born after the date from which the prohibition on the feeding of animal proteins to ruminants became effective. In that case a health certificate should be provided issued by an official veterinarian certifying that they were produced in conformity with this proposed Regulation. Imports of rendered fats and its derivatives into the EC (for food and feed use) from countries placed in category 5 is prohibited unless they were produced from discrete adipose tissue or from material processed according to the standards of Decision 1999/534/EC.

The proposal does not apply to cosmetic or medicinal products and products not destined for human food, animal feed or fertilizers.

Regulation 2001/1248/EC amends Regulation 2001/999/EC w.r.t. the BSE monitoring system in the EC Member States and the information to be provided by Member States on this.

Regulation 2001/1326/EC postpones the implementation of several provisions of Regulation 2001/999/EC. It provisionally defines a list of SRM's to be removed. Imports of these SRM's and products derived therefrom for use in food, animal feed and organic fertilizers will be prohibited. Amends Annex XI of Regulation 2001/999/EC by restricting the importation of rendered fats from third countries to require a health certificate stating a.o.that SRM has been removed, unless the importing country is a country provisionally classified as Category I w.r.t. TSE risks. Restricts the definition of "products of animal origin" to listed products (such as rendered fats) not concerning other products derived from such products of animal origin (such as derivatives of rendered fats).

Regulation 2002/270/EC amends Regulations 2001/999/EC and 2001/1326/EC by amending the provisions for ovine and caprine animals and products derived therefrom. Adds mesentery (adipose tissue from certain parts of the digestive tract) of bovine animals to the provisional list of SRM's in Regulation 2001/999/EC.

Regulation 2002/1494/EC further amends a number of Annexes of Regulation 2001/999/EC by providing a.o. an updated list of countries classified by the Commission as a category I country with regards to TSE risks. In these countries SRM removal is not required.



3.5 BSE/TSE legislation on the export of tallow and tallow derivatives from the UK and Portugal.

Directive 98/256/EC sets the conditions for the export of tallow and tallow derivatives from the UK for use in food, animal feed, cosmetic and pharmaceutical applications. Requires a.o. the removal of SRM and vertebral column at the slaughter house. Animals of over 30 month of age (OTMS animals) cannot be used for tallow production. According to local UK policy, “SRM” and “OTMS” tallow cannot be used for any purpose.

Directive 98/653/EC sets conditions for the export until 1 August 1999 to EC and third countries of products which are liable to enter the food and feed chain and materials destined for use in cosmetics and medicinal products when derived from bovine animals slaughtered in Portugal. Amended by Decision 2000/104/EC extending the export ban in Portugal.

4. TALLOW

4.1 Background

Rendered and melted animal fats account for more than 15% of the total world oils and fats production of 89 million tonnes. Tallow is used in a broad range of applications from shortenings, frying fats and margarine to animal and pet feeds, and in the manufacture of oleochemical products for a very wide variety of applications including food, feed, cosmetics, medicinal and pharmaceutical products.

Tallow is statistically one of the most important animal fats. It is primarily extracted from tissues of bovine and ovine origin although tissues of porcine origin may also be used.

European production of animal fats is around 1.35 million tonnes per annum, a shortfall of around 35% versus usage. Europe is therefore a net importer of tallow. Producers of tallow derivatives, which include soaps, therefore use tallow of both European origin and tallow imported from third countries. Tallow is primarily available from North America (USA, Canada), Australia, New Zealand, and South America (Argentina, Brazil).

4.2 Production of Tallow

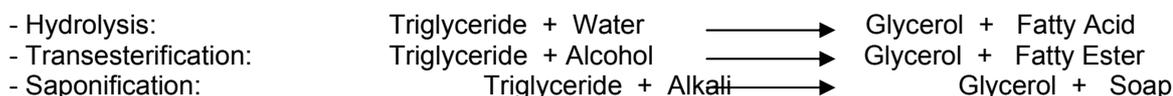
Tallow is extracted from animal tissues containing fat by a variety of processes called rendering or melting. Typically the raw materials are heated, mechanically agitated, and the moisture evaporated or separated. The lipid fraction is separated from the tissues and proteinaceous matter by pressing, centrifugation and filtration. The EU Scientific Steering Committee adopted on 26-27th March the following definition of an appropriate purification process - “one that consists of adequate filtering and/ or centrifugation and/or coagulation and should result in maximum levels of remaining total insoluble impurities of 0.10-0.15% in weight or residual nitrogen below 0.02%, and if possible the residual peptides or polypeptides should have a molecular weight below 10.000 Dalton”.

Process conditions may vary according to the type and quality of the raw materials and the desired quality characteristics of the end product. All European production is via processes equivalent to those listed in the animal by-products Regulation 2001/1774/EC. All imported tallow is also understood to be produced using equivalent processes and additionally is regulated by Council Directive 92/118/EC and the animal by-products Regulation 2001/1774/EC to prevent disease.

5. PROCESSES USED IN THE PRODUCTION OF TALLOW DERIVATIVES

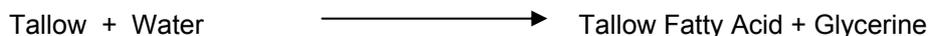
5.1 General

The production of primary derivatives of tallow is achieved through the cleavage of the triglyceride molecule by means of saponification, hydrolysis and transesterification. The resultant products are soaps, fatty acids and fatty esters respectively. Glycerol is a by-product in each case.





5.2 Fatty Acid production via Hydrolysis at high temperature and pressure



The basic hydrolysis process involves the reaction of an oil or fat (in this case tallow) with an excess of water under conditions of high temperature (typically 220°C up to 250°C) and pressure for typically 1.5 to 10 hours (depending on the process equipment) to produce a crude fatty acid and dilute crude glycerol. Pressure is applied to the system, sufficient to maintain the water in the liquid state throughout the reaction and is typically 5 to 10 bars above the saturated vapour pressure of water at the operating temperature. The pressure will therefore vary depending on the operating temperature and is typically 30 to 50 bars at operating temperatures of 220°C to 250°C.

Apart from maintaining liquid conditions in the hydrolysis equipment pressure does not affect the equilibrium state or the rate of the reaction. The crude fatty acid is then distilled at low pressure at about 200°C to remove impurities, including any residual proteinaceous matter and any unsplit fat. The condensed fatty acid vapours yield a high purity, light coloured fatty acid. These conditions far exceed the minimum inactivation conditions (described in paragraph 4.1 and/or in 4.2 above) to inactivate BSE and Scrapie active species, even before distillation.

The broad cut fatty acid may then be hydrogenated under high temperature and pressure to reduce the level of unsaturation and may be fractionally distilled to produce single chain length fractions (e.g. palmitic and pure stearic acids).

Fatty acids can be further processed to give a range of fatty acid derivatives. Examples of fatty acid derivatives are:

Fatty Alcohols_which may be produced directly from fatty acids via catalytic hydrogenation at high temperatures (in excess of 200°C) and at high pressure. The crude alcohol is then distilled (with condensation from the vapour phase) to remove trace impurities. The fatty alcohol may then be fractionally distilled to produce single chain fatty alcohols (e.g. cetyl and stearyl alcohols).

Fatty alcohols_may also be produced indirectly from fatty acids via esterification, (to produce the methyl ester), followed by high temperature, high pressure catalytic hydrogenation.

Metallic Soaps: The basic metallic soap process involves the neutralisation of fatty acids and the appropriate hydroxide.

Fatty Amines: Fatty acids and ammonia are reacted at temperatures of 250°C to 300°C at more than 1.5 bar for more than 5 hours to produce fatty nitriles. These are further processed to produce monoalkyl primary fatty amines, dialkyl and trialkyl secondary and tertiary amines at temperatures above 150°C and contact times of several hours.

Fatty acid esters: These are produced by reacting the tallow fatty acid with an alcohol at temperatures in excess of 200°C. A flowsheet for the manufacture of esters from rendered fats which are used in critical applications like animal feed, cosmetics and pharmaceuticals is given in Annex I to this report.

Fatty amides are produced by the reaction of ammonia with fatty acids at around 200°C.

5.3 Fatty Alcohol production via transesterification at high temperature and pressure

Tallow is converted to tallow methyl ester by high temperature (in excess of 200°C), high pressure transesterification with methanol (reaction time in excess of 20 minutes). As in hydrolysis pressure plays no part in the reaction other than to maintain the methanol in the liquid state throughout the reaction. Typically at 200°C the pressure will be at least 40 bar.



The methyl ester is then distilled to remove water and trace impurities, including any residual proteinaceous material and trace quantities of glycerine, before hydrogenation. The distilled methyl ester is then hydrogenated in either the liquid or vapour phase at temperatures in excess of 200°C. The tallow fatty alcohol produced in the liquid phase is then distilled to remove any unconverted ester and other trace impurities.



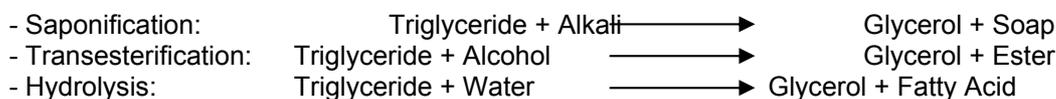


Cetyl and Stearyl Alcohols may be produced by fractional distillation of the tallow alcohol (or from fractionated tallow methyl esters).

These process conditions are at least equal, and typically far exceed, the inactivation conditions described above. It follows that Fatty Alcohols produced via the above conditions for transesterification can be considered safe for any use, including food, animal feed, and medicinal, pharmaceutical and cosmetics products, regardless of the source of the tallow used and regardless of the type of material used in the production of that tallow.

5.4 Glycerol Production

Each of the three basic processes for producing tallow derivatives produce glycerol through cleavage of the triglyceride molecule (i.e. saponification, transesterification or hydrolysis).



The crude glycerol produced from the above reactions undergoes considerably more processing to produce the pure high quality glycerine used in food, cosmetics and pharmaceutical products.

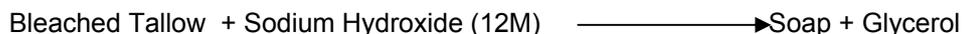
5.4.1 Crude Glycerol production

A) Crude glycerol from saponification - hydrolysis at high alkalinity

The process of manufacture of soap and crude glycerol from blends of oils and fats (tallow) involves bleaching followed by saponification (hydrolysis at high alkalinity) of the blend under conditions of high temperature and alkalinity. Depending on the type of saponification process either elevated pressure or extended manufacturing times are also factors. The separated soap is then further concentrated via a heat exchange process.

The "bleaching" process involves heating the oil or fat for typically 45 minutes to about 100°C in the presence of bleaching earth followed by filtration. The filtration process should ensure complete removal of any trace quantities of solid impurities thus further reducing any negligible possibility that TSE agents could survive through to the second and much more aggressive stage, saponification.

The saponification process involves reacting the oils and fats with sodium hydroxide:



The saponification process can take place via two alternative routes, both of which are widely used.

1) Typical Process for Continuous Saponification operating in the industry

The bleached oil/fat blend is heated to 105°C and mixed with sodium hydroxide before entering a saponification reaction column. In this stage an exothermic reaction takes place as the oil/fat (tallow) blend is mixed with 12 M sodium hydroxide at a temperature of about 140°C under a pressure of about 2 bar. Residence time is a minimum of 8 minutes. It is normal to verify at frequent intervals that all the fatty material has reacted by confirming that the soap still contains free alkali. Further confirmation is obtained by monitoring the temperature profile through the process. As it is an exothermic reaction a stabilised process temperature confirms that the reaction is complete. The glycerol is then washed out of the soap mass and concentrated giving typically another 1.5 hours (average 3.5 hours) exposure to alkaline conditions at a temperature up to 140°C.

Equivalent conditions may be used where the saponification process is carried out at a slightly lower temperature but for extended time periods. Carried out to the extreme this equates to the batch process described below.



2) Typical Process for Batch Saponification operating in the industry

In this case soap is produced in a pan where again it is reacted with 12 M sodium hydroxide at 95°C typically for a period of 3 hours. The soap and glycerol is kept at this high temperature for up to 5 days under slightly alkaline conditions to complete the washing process and separation of the glycerine.

B) Crude glycerol from the transesterification and hydrolysis (high temperature, high pressure) processes.

In the transesterification process described earlier the residence time for the glycerol is at least 20 minutes at a minimum of 200°C.

In the hydrolysis process also described earlier the residence time for the glycerol can range from a minimum of 30 minutes to over 10 hours at temperatures in excess of 200°C depending on the process used.

Thus, in all cases the crude glycerol has at various stages in its production been exposed to recognised inactivation conditions as described in the opinions in Chapter 2.1 above.

It should follow that crude glycerol, derived from tallow and produced via saponification, transesterification and hydrolysis processes and conditions described above, can be considered safe regardless of the source of the tallow used and regardless of the type of material used in the production of that tallow.

However, crude glycerol from the above reactions undergoes considerably more processing to produce the pure high quality glycerol used in food, medicinal, pharmaceutical and cosmetic products.

5.4.2. Pure glycerol production

Two basic methods are used:

(i) evaporation, pre-treatment, concentration, and *distillation* followed by carbon bleaching and filtration.

(ii) evaporation, pre-treatment, *ion exchange*, and concentration, followed by carbon bleaching and filtration. Some companies add a distillation step after concentration.

The Distillation Process

Crude glycerol from saponification, transesterification and hydrolysis can be purified following this route. Where necessary the dilute glycerol is treated to remove impurities such as protein degradation products, and fatty acids. The chemicals commonly used are aluminium and iron salts as coagulants, hydrochloric acid and caustic. The pre-treated material is filtered using filter aids and is then concentrated up to 99% (if necessary) before distillation. The concentrated glycerol is then distilled under vacuum at temperatures of about 160°C for further purification. The distilled glycerol (99.5-99.9%) is condensed from the vapour stream and then treated with carbon to adsorb trace impurities such as colour and odour bodies and finally filtered to remove any remaining particulate material.

The Ion Exchange Process

Purification of glycerol containing low salt levels such as that recovered from interesterification and hydrolysis reactions can also be carried out using ion exchange followed by evaporation/concentration. After partial concentration and simple pre-treatment, salts, acids and pigments are removed from the dilute glycerol (using modern filter presses or centrifuges) which is then passed through vessels containing special ion exchange resin granules. The ion exchange units operate in pairs with each unit consisting of an anion and a cation exchanger so that positively and negatively charged impurities are held back and purified glycerol ready for evaporation/concentration emerges. The exchangers are installed to also retain traces of fat, soaps, proteins and other impurities. The purified glycerol is then concentrated up to 99.5-99.9% glycerol before treatment with carbon to adsorb trace impurities such as residual colour and odour bodies and is finally filtered to remove any remaining particulate material.

These further glycerol refining processes serve to improve the purity of the product and further support the conclusion that glycerol produced from tallow is safe for its intended use.



6. HAZARD ANALYSIS OF CRITICAL CONTROL POINTS.

Hazard Analysis Critical Control Points (HACCP) is a quality assurance management tool which focuses on control of Critical Control Points in the manufacture certain products. Application of the HACCP tool is currently only mandatory by EC Directive 93/43/EEC in the manufacture of food and food ingredients. HACCP will most likely become mandatory in the manufacture of oils and fats (and materials derived therefrom) intended for animal feed as proposed in SANCO 2741/99 Rev 7 on prohibited ingredients in animal nutrition. Following Decision 2003/326/EC amending the animal by-products Regulation 2002/1774/EC, HACCP will be required by 31st October 2005, HACCP on the processes outlined in Section 5.1. of this report.

Introduction of GMP/HACCP practices in the manufacture of pharmaceutical excipients is under discussion. Certificates of Suitability w.r.t. BSE for pharmaceutical ingredients will only be issued if GMP/HACCP practices are in place.

HACCP involves the systematic examination of process steps and the identification of those steps that are critical to the safety of the product (i.e. Critical Control Points: CCP's). A correctly completed HACCP study can identify all currently conceivable product safety hazards, together with a list of CCP's and related limits, monitoring procedures and corrective actions, to be verified on a regular basis and be updated when changes occur.

HACCP is applicable to the identification of microbiological, chemical and physical hazards affecting the safety of the product. HACCP must be applied to a specific process - product combination and should make use of existing information, such as GMP guidelines, relevant to the product/process under study. HACCP requires full commitment of senior management and technical staff to provide the resources necessary for completion of the study and implementation of the recommendations.

HACCP will enable management to maintain an effective ongoing safety programme. HACCP identifies potential hazards and implements preventive controls in the manufacture environment and as such is a cornerstone of any quality assurance policy.

7. CONCLUSIONS ON THE SAFETY OF TALLOW DERIVATIVES.

For the safety of tallow derivatives with respect to transmission of spongiform encephalopathy the scientific opinions as expressed by the Scientific Steering Committee on the process conditions for the manufacture of these derivatives and the legal framework within which APAG members have to operate are relevant:

With respect to scientific opinions it can be concluded that:

The rigorous processes used by APAG members in the production of tallow derivatives for use in food, feed, medicinal, pharmaceutical and cosmetic products, comply with the recognised conditions for inactivating the BSE agent as defined by the EU Scientific Steering Committee in various opinions since March 1998.

The safety of tallow derivatives is further supported by the legal framework adopted or proposed with which APAG members have to comply as follows:

For food and food ingredients: following Regulation 2001/999/EC and its amendments (Regulations 2001/1326/EC and 2002/270/EC) tallow must be obtained from animals fit for human consumption and should not be derived in whole or in part from Specified Risk Material if sourced from an EU Member State or from a third country not provisionally classified in GBR I. The animal by-products Regulation 2002/1774/EC covers animal by-products not intended for human consumption. Tallow intended for food applications is Regulated by Directive 77/99/EEC and its subsequent amendments. Imports of tallow for human consumption is Regulated by the "Balai" Directive 92/118/EC.

For animal feed: following Regulation 2001/999/EC and its amendments (Regulations 2001/1326/EC and 2002/270/EC) tallow must be obtained from animals fit for human consumption and should not be derived in whole or in part from Specified Risk Material if sourced from an EU Member State or from a third country not provisionally classified in GBR I.



The animal by-products Regulation 2002/1774/EC requires the use category 3 tallow for the manufacture of tallow derivatives. After 31 December 2003 imported tallow derivatives destined for feed must also be derived from category 3 tallow as evidenced by an import certificate.

Pharmaceutical ingredients: The animal by-products Regulation 2002/1774/EC requires the use category 3 tallow for the manufacture of tallow derivatives. After 31 December 2003 imported tallow derivatives destined for pharmaceutical applications must also be derived from category 3 tallow as evidenced by an import certificate.

Cosmetic ingredients: The animal by-products Regulation 2002/1774/EC requires the use category 3 tallow for the manufacture of tallow derivatives. After 31 December 2003 imported tallow derivatives destined for use in cosmetic formulations must also be derived from category 3 tallow as evidenced by an import certificate.

Industrial applications: The animal by-products Regulation 2002/1774/EC requires as a minimum the use of category 2 tallow for the manufacture of tallow derivatives for industrial applications (i.e. not for food, animal feed, cosmetics and pharmaceuticals). Tallow derived in whole or in part from Specified Risk Material cannot be used. After 31 December 2003 imported tallow derivatives destined for industrial applications must also be derived from category 2 tallow as evidenced by an import certificate.

8. REFERENCES

1. Scientific Steering Committee opinion on "The safety of tallow derived from ruminant tissues", March 1998.
2. Scientific Steering Committee opinion on "The risks of non conventional transmissible agents (BSE), conventional infectious agents or other hazards such as toxic substances entering the human food or animal feed chains via raw material from fallen stock and dead animals or via condemned animals" June 1999.
3. Scientific Steering Committee "Opinion on the safety with regard to BSE of certain bovine tissues and certain animal-derived products", January 2001.
4. Scientific Steering Committee "Revised opinion and report on the safety of tallow from ruminant slaughter by-products", June 2001.
5. Scientific Steering Committee "Opinion on the hypothesis on the origin and transmission of BSE", November 2001.
6. Scientific Steering Committee "Opinion on the safety of tallow derivatives from cattle tallow", April 2003.
7. WHO/CDS/VPH/95.145 Report of a World Health Organisation consultation on public health issues related to human & animal transmissible spongiform encephalopathies, 17-19 May 1995.
8. EC Committee on Proprietary Medicinal Products, Minimising the risk of transmitting agents causing spongiform encephalopathy via medicinal products, 1992 & EMEA Press Release dated 18th April 1997 covering the CPMP plenary meeting in April 1997.
9. Committee on Proprietary Medicinal Products report "Note for guidance on minimising the risks of transmitting TSE agents via human and veterinary medicinal products", February 2001.
10. Scientific Committee on Cosmetology's opinion given at their meeting in June 1997
11. Scientific Committee on Cosmetic Products and Non-Food Products intended for consumers opinion concerning "Amendment to entry 419 of Annex II to Directive 76/768/EC on cosmetic products", adopted in December 2002.
12. Inactivation of the bovine spongiform encephalopathy agent by rendering processes.
D.M. Taylor, S.L. Woodgate, M.J. Atkinson. The Veterinary Record, December 9 1995, 137, 605-610. TSE Agents: Inactivation by rendering systems and the role of inactivation research on new processing regulations for the European Rendering Industry. Paper from S. Woodgate to Lipidex 97 Symposium, Antwerp, 18-21st March 1997.
13. Press Release WHO/28 - 3 April 1996. Rev.1 (15 April 1996)
14. D.Riesner et al, J.Gen.Virol. 82, 465 – 473, 2001