Amendments to relevant sections of the summary of product characteristics and package leaflet, as approved by the CHMP on 13 December 2012, pending endorsement by the European Commission

Tisseel and associated names

A. Summary of Products Characteristics

The following changes should be made to the SmPC of Tisseel and associated names:

4.2 Posology and method of administration

The following text should be added to this section:

"The use of [PRODUCT NAME] is restricted to experienced surgeons who have been trained in the use of [PRODUCT NAME]."

4.2.2 Method and route of administration

This section of the SmPC should include the following wording:

"In order to ensure optimal safe use of [PRODUCT NAME] by spray application the following recommendations should be followed:

In open wound surgery - a pressure regulator device that delivers a maximum pressure of no more than 2.0 bar (28.5 psi) should be used.

In minimally invasive/laparoscopic procedures – a pressure regulator device that delivers a maximum pressure of no more than 1.5 bar (22 psi) and uses carbon dioxide gas only should be used.

Prior to applying [PRODUCT NAME] the surface area of the wound needs to be dried by standard techniques (e.g. intermittent application of compresses, swabs, use of suction devices).

[PRODUCT NAME] should only be reconstituted and administered according to the instructions and with the devices recommended for this product (see section 6.6).

For spray application, see sections 4.4 and 6.6 for specific recommendations on the required pressure and distance from tissue per surgical procedure and length of applicator tips."

4.4 Special warnings and precautions for use

This section of the SmPC should include the following wording, in bold and underlined format where indicated:

*"**Apply [PRODUCT NAME] as a thin layer. Excessive clot thickness may negatively interfere with the product's efficacy and the wound healing process.***

Life-threatening/fatal air or gas embolism has occurred with the use of spray devices employing a pressure regulator to administer fibrin sealants. This event appears to be related to the use of the spray device at higher than recommended pressures and/or in close proximity to the tissue surface. The risk appears to be higher when fibrin sealants are sprayed with air, as compared to CO_2 and therefore cannot be excluded with [Product Name] when sprayed in open wound surgery.

When applying [PRODUCT NAME] using a spray device, be sure to use a pressure within the pressure range recommended by the spray device manufacturer (see table in section 6.6 for pressures and distances).

[PRODUCT NAME] spray application should only be used if it is possible to accurately judge the spray distance as recommended by the manufacturer. Do not spray closer than the recommended distances.

When spraying [PRODUCT NAME], changes in blood pressure, pulse, oxygen saturation and end tidal CO_2 should be monitored because of the possibility of occurrence of air or gas embolism (also see section 4.2).*"*

6.6 Special precautions for disposal

Spray application

This section of the SmPC should include the following wording, in bold and underlined format where indicated:

"When applying [PRODUCT NAME] using a spray device be sure to use a pressure and a distance from tissue within the ranges recommended by the manufacturer as follows:

Recommended pressure, distance and devices for spray application of [product name]					
Surgery	*Spray set to be used*	*Applicator tips to be used*	*Pressure regulator to be used*	*Recommended distance from target tissue*	*Recommended spray pressure*
Open wound	*Tisseel / Artiss Spray Set*	*n.a.*	*EasySpray*	*10-15cm*	*1.5-2.0 bar (21.5-28.5 psi).*
	Tisseel / Artiss Spray Set 10 pack	*n.a.*	*EasySpray*		
Laparoscopic/ minimally invasive procedures	*n.a.*	*Duplospray MIS Applicator 20cm*	*Duplospray MIS Regulator*	*2 – 5 cm*	*1.2-1.5 bar (18-22 psi)*
			Duplospray MIS Regulator NIST B11		
		Duplospray MIS Applicator 30cm	*Duplospray MIS Regulator*		
			Duplospray MIS Regulator NIST B11		
		Duplospray MIS Applicator 40cm	*Duplospray MIS Regulator*		
			Duplospray MIS Regulator NIST B11		
		Replaceable tip	*Duplospray MIS Regulator*		
			Duplospray MIS Regulator NIST B11		

When spraying the [PRODUCT NAME], changes in blood pressure, pulse, oxygen saturation and end tidal CO_2 should be monitored because of the possibility of occurrence of air or gas embolism (see sections 4.2 and 4.4).*"*

B. Package Leaflet

The following changes should be made to the package leaflet of Tisseel and associated names:

2. Before you use [PRODUCT NAME]

Take special care with **[PRODUCT NAME]**

This section of the Package Leaflet should include the following wording, in bold and underlined format where indicated:

- ***"Life-threatening/fatal air or gas embolism (air getting into the blood circulation which can be serious or life-threatening) has occurred very rarely with the use of spray devices employing pressure regulators to administer fibrin sealants. This appears to be related to the use of the spray device at higher than recommended pressures and/or in close proximity to the tissue surface. The risk appears to be higher when fibrin sealants are sprayed with air, as compared to CO_2 and therefore cannot be excluded with [Product Name] when sprayed in open wound surgery.***
- ***Spray devices and the accessory tip provide instructions for use with recommendations for pressure ranges and to the spraying distance from the tissue surface.***
- ***[PRODUCT NAME] should be administered strictly according to the instructions and only with devices recommended for this product.***
- ***When spraying [PRODUCT NAME], changes in blood pressure, pulse, oxygen saturation and end tidal CO_2 should be monitored for possible occurrence of gas embolism."***

3. How to use [PRODUCT NAME]

This section of the Package Leaflet should include the following wording, in bold and underlined format where indicated:

"The use of [PRODUCT NAME] is restricted to experienced surgeons who have been trained in the use of [PRODUCT NAME]

Prior to applying [PRODUCT NAME] the surface area of the wound needs to be dried by standard techniques (e.g. intermittent application of compresses, swabs, use of suction devices).

When applying [PRODUCT NAME] using a spray device be sure to use a pressure and a distance from the tissue within the range recommended by the manufacturer as follows:

Recommended pressure, distance and devices for spray application of [product name]					
Surgery	*Spray set to be used*	*Applicator tips to be used*	*Pressure regulator to be used*	*Recommended distance from target tissue*	*Recommended spray pressure*
Open wound	*Tisseel / Artiss Spray Set*	*n.a.*	*EasySpray*	*10-15cm*	*1.5-2.0 bar (21.5-28.5 psi).*
	Tisseel / Artiss Spray Set 10 pack	*n.a.*	*EasySpray*		
Laparoscopic/ minimally invasive procedures	*n.a.*	*Duplospray MIS Applicator 20cm*	*Duplospray MIS Regulator*	*2 – 5 cm*	*1.2-1.5 bar (18-22 psi)*
			Duplospray MIS Regulator NIST B11		
		Duplospray MIS Applicator 30cm	*Duplospray MIS Regulator*		
			Duplospray MIS Regulator NIST B11		
		Duplospray MIS Applicator 40cm	*Duplospray MIS Regulator*		
			Duplospray MIS Regulator NIST B11		
		Replaceable tip	*Duplospray MIS Regulator*		
			Duplospray MIS Regulator NIST B11		

When spraying the [PRODUCT NAME], changes in blood pressure, pulse, oxygen saturation and end tidal CO_2 should be monitored because of the possibility of occurrence of air or gas embolism (see section 2)."

Tissucol and associated names

A. Summary of Products Characteristics

The following changes should be made to the SmPC of Tissucol and associated names:

4.2 Posology and method of administration

The following text should be added to this section:

"The use of [PRODUCT NAME] is restricted to experienced surgeons who have been trained in the use of [PRODUCT NAME]."

4.2.2 Method and route of administration

This section of the SmPC should include the following wording:

"In order to ensure optimal safe use of [PRODUCT NAME] by spray application the following recommendations should be followed:

In open wound surgery - a pressure regulator device that delivers a maximum pressure of no more than 2.0 bar (28.5 psi) should be used.

In minimally invasive/laparoscopic procedures – a pressure regulator device that delivers a maximum pressure of no more than 1.5 bar (22 psi) and uses carbon dioxide gas only should be used.

Prior to applying [PRODUCT NAME] the surface area of the wound needs to be dried by standard techniques (e.g. intermittent application of compresses, swabs, use of suction devices).

[PRODUCT NAME] should only be reconstituted and administered according to the instructions and with the devices recommended for this product (see section 6.6).

For spray application, see sections 4.4 and 6.6 for specific recommendations on the required pressure and distance from tissue per surgical procedure and length of applicator tips."

4.4 Special warnings and precautions for use

This section of the SmPC should include the following wording, in bold and underlined format where indicated:

"Apply [PRODUCT NAME] as a thin layer. Excessive clot thickness may negatively interfere with the product's efficacy and the wound healing process.

Life-threatening/fatal air or gas embolism has occurred with the use of spray devices employing a pressure regulator to administer fibrin sealants. This event appears to be related to the use of the spray device at higher than recommended pressures and/or in close proximity to the tissue surface. The risk appears to be higher when fibrin sealants are sprayed with air, as compared to CO_2 and therefore cannot be excluded with [Product Name] when sprayed in open wound surgery.

When applying [PRODUCT NAME] using a spray device, be sure to use a pressure within the pressure range recommended by the spray device manufacturer (see table in section 6.6 for pressures and distances).

[PRODUCT NAME] spray application should only be used if it is possible to accurately judge the spray distance as recommended by the manufacturer. Do not spray closer than the recommended distances.

When spraying [PRODUCT NAME], changes in blood pressure, pulse, oxygen saturation and end tidal CO_2 should be monitored because of the possibility of occurrence of air or gas embolism (also see section 4.2).*"*

6.6 Special precautions for disposal

Spray application

This section of the SmPC should include the following wording, in bold and underlined format where indicated:

"When applying [PRODUCT NAME] using a spray device be sure to use a pressure and a distance from tissue within the ranges recommended by the manufacturer as follows:

Recommended pressure, distance and devices for spray application of [product name]					
Surgery	*Spray set to be used*	*Applicator tips to be used*	*Pressure regulator to be used*	*Recommended distance from target tissue*	*Recommended spray pressure*
Open wound	*Duploject Spray Set*	*n.a.*	*Tissomat*	*10-15cm*	*1.5-2.0 bar (21.5-28.5 psi).*
	Tisseel / Tissucol Spray Set	*n.a.*	*EasySpray*	*10-15cm*	*1.5-2.0 bar (21.5-28.5 psi).*
Laparoscopic/ minimally invasive procedures	*n.a.*	*Duplospray MIS Applicator 20cm*	*Duplospray MIS Regulator*	*2 – 5 cm*	*1.2-1.5 bar (18-22 psi)*
			Duplospray MIS Regulator NIST B11		
		Duplospray MIS Applicator 30cm	*Duplospray MIS Regulator*		
			Duplospray MIS Regulator NIST B11		
		Duplospray MIS Applicator 40cm	*Duplospray MIS Regulator*		
			Duplospray MIS Regulator NIST B11		
		Replaceable tip	*Duplospray MIS Regulator*		
			Duplospray MIS Regulator NIST B11		

When spraying the [PRODUCT NAME], changes in blood pressure, pulse, oxygen saturation and end tidal CO_2 should be monitored because of the possibility of occurrence of air or gas embolism (see sections 4.2 and 4.4)."

B. Package Leaflet

The following changes should be made to the package leaflet of Tissucol and associated names:

2. Before you use [PRODUCT NAME]

***Take special care with* [PRODUCT NAME]**

This section of the Package Leaflet should include the following wording, in bold and underlined format where indicated:

- ***"Life-threatening/fatal air or gas embolism (air getting into the blood circulation which can be serious or life-threatening) has occurred very rarely with the use of spray devices employing pressure regulators to administer fibrin sealants. This appears to be related to the use of the spray device at higher than recommended pressures and/or in close proximity to the tissue surface. The risk appears to be higher when fibrin sealants are sprayed with air, as compared to CO_2 and therefore cannot be excluded with [Product Name] when sprayed in open wound surgery.***
- ***In minimally invasive/laparoscopic procedures: spray application of [Product Name] should be with a pressure regulator that only employs carbon dioxide***
- ***Spray devices and the accessory tip provide instructions for use with recommendations for pressure ranges and to the spraying distance from the tissue surface.***
- ***[PRODUCT NAME] should be administered strictly according to the instructions and only with devices recommended for this product.***
- ***When spraying [PRODUCT NAME], changes in blood pressure, pulse, oxygen saturation and end tidal CO_2 should be monitored for possible occurrence of gas embolism.***

3. How to use [PRODUCT NAME]

This section of the Package Leaflet should include the following wording, in bold and underlined format where indicated:

"The use of [PRODUCT NAME] is restricted to experienced surgeons who have been trained in the use of [PRODUCT NAME]

Prior to applying [PRODUCT NAME] the surface area of the wound needs to be dried by standard techniques (e.g. intermittent application of compresses, swabs, use of suction devices).

When applying [PRODUCT NAME] using a spray device be sure to use a pressure and a distance from the tissue within the range recommended by the manufacturer as follows:

Recommended pressure, distance and devices for spray application of [product name]					
Surgery	*Spray set to be used*	*Applicator tips to be used*	*Pressure regulator to be used*	*Recommended distance from target tissue*	*Recommended spray pressure*
Open wound	*Duploject Spray Set*	*n.a.*	*Tissomat*	*10-15cm*	*1.5-2.0 bar (21.5-28.5 psi).*
	Tisseel / Tissucol Spray Set	*n.a.*	*EasySpray*	*10-15cm*	*1.5-2.0 bar (21.5-28.5 psi).*
Laparoscopic/ minimally invasive procedures	*n.a.*	*Duplospray MIS Applicator 20cm*	*Duplospray MIS Regulator*	*2 – 5 cm*	*1.2-1.5 bar (18-22 psi)*
			Duplospray MIS Regulator NIST B11		
		Duplospray MIS Applicator 30cm	*Duplospray MIS Regulator*		
			Duplospray MIS Regulator NIST B11		
		Duplospray MIS Applicator 40cm	*Duplospray MIS Regulator*		
			Duplospray MIS Regulator NIST B11		
		Replaceable tip	*Duplospray MIS Regulator*		
			Duplospray MIS Regulator NIST B11		

When spraying the [PRODUCT NAME], changes in blood pressure, pulse, oxygen saturation and end tidal CO_2 should be monitored because of the possibility of occurrence of air or gas embolism (see section 2)."

Artiss

A. Summary of Products Characteristics

The following changes should be made to the SmPC of Artiss:

4.2 Posology and method of administration

This wording:

"ARTISS is intended for Hospital Use Only by suitably experienced physicians or surgeons."

Should be replaced by:

"The use of [PRODUCT NAME] is restricted to experienced surgeons who have been trained in the use of [PRODUCT NAME]."

4.2.2 Method and route of administration

This section of the SmPC should include the following wording:

"For subcutaneous use only. [PRODUCT NAME] is not recommended for laparoscopic surgery.

In order to ensure optimal safe use of [PRODUCT NAME] it should be sprayed using a pressure regulator device that delivers a maximum pressure of up to 2.0 bar (28.5 psi).

Prior to applying [PRODUCT NAME] the surface area of the wound needs to be dried by standard techniques (e.g. intermittent application of compresses, swabs, use of suction devices).

[PRODUCT NAME] should only be reconstituted and administered according to the instructions and with the devices recommended for this product (see section 6.6).

For spray application, see sections 4.4 and 6.6 for specific recommendations on the required pressure and distance from tissue per surgical procedure and length of applicator tips."

4.4 Special warnings and precautions for use

This section of the SmPC should include the following wording, in bold and underlined format where indicated:

*"**Apply [PRODUCT NAME] as a thin layer. Excessive clot thickness may negatively interfere with the product's efficacy and the wound healing process.***

Life-threatening air or gas embolism has occurred with the use of spray devices employing a pressure regulator to administer fibrin sealants. This event appears to be related to the use of the spray device at higher than recommended pressures and/or in close proximity to the tissue surface. The risk appears to be higher when fibrin sealants are sprayed with air, as compared to CO_2 and therefore cannot be excluded with [PRODUCT NAME].

When applying [PRODUCT NAME] using a spray device, be sure to use a pressure within the pressure range recommended by the spray device manufacturer (see table in section 6.6 for pressures and distances).

<u>[PRODUCT NAME] spray application should only be used if it is possible to accurately judge the spray distance as recommended by the manufacturer. Do not spray closer than the recommended distances.</u>

<u>When spraying [PRODUCT NAME], changes in blood pressure, pulse, oxygen saturation and end tidal CO_2 should be monitored because of the possibility of occurrence of air or gas embolism (also see section 4.2).</u>*"*

6.6 Special precautions for disposal

<u>Spray application</u>

This section of the SmPC should include the following wording, in bold and underlined format where indicated:

"When applying [PRODUCT NAME] using a spray device be sure to use a pressure and a distance from tissue within the ranges recommended by the manufacturer as follows:

Recommended pressure, distance and devices for spray application of [product name]					
	Spray set to be used	*Applicator tips to be used*	*Pressure regulator to be used*	*Recommended distance from target tissue*	*Recommended spray pressure*
Open wound surgery of subcutaneous tissue	*Tisseel / Artiss Spray Set*	*n.a.*	*EasySpray*	*10 – 15 cm*	*1.5-2.0 bar (21.5-28.5 psi)*
	Tisseel / Artiss Spray Set 10 pack	*n.a.*	*EasySpray*		

<u>When spraying the [PRODUCT NAME], changes in blood pressure, pulse, oxygen saturation and end tidal CO_2 should be monitored because of the possibility of occurrence of air or gas embolism (see sections 4.2 and 4.4)."</u>

B. Package Leaflet

The following changes should be made to the package leaflet of Artiss and associated names:

2. Before you use [PRODUCT NAME]

***Take special care with* [PRODUCT NAME]**

This section of the Package Leaflet should include the following wording, in bold and underlined format where indicated:

- ***"[PRODUCT NAME] should not be used in laparoscopic surgery (keyhole surgery).***
- ***Life-threatening/fatal air or gas embolism (air getting into the blood circulation which can be serious or life-threatening) has occurred very rarely with the use of spray devices employing pressure regulators to administer fibrin sealants. This appears to be related to the use of the spray device at higher than recommended pressures and/or in close proximity to the tissue surface. The risk appears to be higher when fibrin sealants are sprayed with air, as compared to CO_2 and therefore cannot be excluded with [Product Name].***
- ***When [PRODUCT NAME] is applied using a spray device, the pressure and spraying distance have to be within the range recommended by the manufacturer. [PRODUCT NAME] should be administered strictly according to the instructions and only with devices recommended for this product.***
- ***When spraying [PRODUCT NAME], changes in blood pressure, pulse, oxygen saturation and end tidal CO_2 should be monitored for possible occurrence of gas embolism."***

3. How to use [PRODUCT NAME]

This section of the Package Leaflet should include the following wording, in bold and underlined format where indicated:

"The use of [PRODUCT NAME] is restricted to experienced surgeons who have been trained in the use of [PRODUCT NAME].

Prior to applying [PRODUCT NAME] the surface area of the wound needs to be dried by standard techniques (e.g. intermittent application of compresses, swabs, use of suction devices).

When applying [PRODUCT NAME] using a spray device be sure to use a pressure and a distance from the tissue within the range recommended by the manufacturer as follows:

Recommended pressure, distance and devices for spray application of [product name]					
	Spray set to be used	*Applicator tips to be used*	*Pressure regulator to be used*	*Recommended distance from target tissue*	*Recommended spray pressure*
Open wound surgery of subcutaneous tissue	*Tisseel / Artiss Spray Set*	*n.a.*	*EasySpray*	*10 – 15 cm*	*1.5-2.0 bar (21.5-28.5 psi)*
	Tisseel / Artiss Spray Set 10 pack	*n.a.*	*EasySpray*		

When spraying the [PRODUCT NAME], changes in blood pressure, pulse, oxygen saturation and end tidal CO_2 should be monitored because of the possibility of occurrence of air or gas embolism (see section 2)."

Beriplast P and associated names

A. Summary of Products Characteristics

The following changes should be made to the package leaflet of Beriplast P and associated names:

4.2 Posology and method of administration

The following text should be inserted in this section:

"Prior to applying [PRODUCT NAME] the surface area of the wound needs to be dried by standard techniques (e.g. intermittent application of compresses, swabs, use of suction devices).

[PRODUCT NAME] should only be reconstituted and administered according to the instructions and with the devices as provided with this product."

6.6 Special precautions for disposal

The following text should be inserted in this section:

"Prior to applying [PRODUCT NAME] the surface area of the wound needs to be dried by standard techniques (e.g. intermittent application of compresses, swabs, use of suction devices)."

B. Package Leaflet

The following changes should be made to the package leaflet of Beriplast P and associated names:

4. Possible side effects

Section 4.2 – Method and route of administration

The following text should be inserted in this section:

"Prior to applying Beriplast the surface area of the wound needs to be dried by standard techniques (e.g. intermittent application of compresses, swabs, use of suction devices).

The product should only be reconstituted and administered according to the instructions and with the devices as provided with this product."

Section 6.6 – Special precautions for disposal

The following text should be inserted in this section:

"Prior to applying [product name] the surface area of the wound needs to be dried by standard techniques (e.g. intermittent application of compresses, swabs, use of suction devices)."

Information for healthcare professionals

The following text should be inserted in this section:

"Prior to applying Beriplast the surface area of the wound needs to be dried by standard techniques (e.g. intermittent application of compresses, swabs, use of suction devices).

The product should only be reconstituted and administered according to the instructions and with the devices as provided with this product."