21 February 2013
EMA/CHMP/796122/2012
Committee for Medicinal Products for Human Use (CHMP)

Consultation procedure Public Assessment Report (CPAR)

Consultation on an ancillary medicinal substance incorporated in a medical device

Medical device: PureSperm Wash

Ancillary medicinal substance: Human Albumin Solution

EMEA/H/D/2650

Applicant: Det Norske Veritas Certification AS

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8545
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

Table of contents

Administrative information

Invented name of medical device:	PureSperm Wash
INN (or common name) of the ancillary medicinal substance:	Human Albumin Solution
Applicant for medical device CE certification:	NidaCon International AB
Notified body:	Det Norske Veritas Certification AS
Applied intended purpose of the device:	PureSperm Wash is used to extend the ejaculate prior to an intrauterine insemination (IUI), for rinsing or washing human sperm after they have been purified and concentrated on a density gradient, for swim-up preparation and for in vitro storage of sperm.
Intended purpose of the ancillary medicinal substance in the device:	The rinsing and washing processes are done in either a glass or a plastic test tube, and the surfaces of these tubes have an electrical charge and may also have hydrophobic effects. In addition, the sperm all carry a negative charge on their cell surfaces, while also the albumin molecule itself has strong negative charge. The resulting attraction and repulsion effects stop the sperm from sticking to the glass or plastic test tube (adhesion), or to each other (aggregation). This is the principle reason for including albumin in the product.
Pharmaceutical form(s) and strength(s) of the ancillary medicinal substance:	Human Albumin Solution 25% Extracorporeal solution, 5.65 g/ml

1. Background information on the procedure

1.1. Submission of the dossier

The notified body Det Norske Veritas Certification AS submitted to the European Medicines Agency (EMA) on 26 October 2011 an application for consultation for Human Albumin Solution as ancillary medicinal substance used in a medical device PureSperm Wash, in accordance with the procedure falling within the scope of Directive 93/42/EEC, as amended.

Steps taken for the assessment of the product

The Rapporteur and Co-Rapporteur appointed by the CHMP and the evaluation teams were:

Rapporteur: Kristina Dunder Co-Rapporteur: Ian Hudson

- The application was received by the EMA on 26/10/2011.
- The procedure started on 21/12/2011.
- The Rapporteur's first assessment report was circulated to all CHMP members on 09/03/2012. The Co-Rapporteur's first assessment report was circulated to all CHMP members on 23/02/2012.
- During the meeting on 16-19/04/2012, the CHMP agreed on the consolidated list of questions to be sent to the applicant. The final consolidated list of questions was sent to the applicant on 20/04/2012.
- The applicant submitted the responses to the CHMP consolidated list of questions on 11/10/2012.
- The Rapporteurs circulated the joint assessment report on the applicant's responses to the list of questions to all CHMP members on 23/11/2012.
- During the CHMP meeting on 10-13/12/2012, the CHMP agreed on a list of outstanding issues to be addressed in writing by the applicant.
- The applicant submitted the responses to the CHMP consolidated list of outstanding issues on 21/01/2013.
- The Rapporteurs circulated the joint assessment report on the applicant's responses to the list of outstanding issues to all CHMP members on 29 January 2013.
- During the meeting on 18-21/02/2013, the CHMP, in the light of the overall data submitted and the scientific discussion within the committee, issued a positive opinion on the quality and safety including the clinical benefit/risk profile of Human Albumin Solution used as ancillary medicinal substance in Pure Sperm Wash on 21/02/2013.

1.2. Manufacturers

Manufacturers of the active substance used as ancillary medicinal substance

Octapharma Pharmazeutika Produktionges.m.b.H.
Oberlaaer Strabe 235, A-1100 Vienna
Austria

Octapharma AB
Elersvagen 40, SE-112 75 Stockholm
Sweden

Manufacturing licences dated 13-14/12/2010 and 05/03/2010 respectively were provided.

Manufacturers responsible for batch release

Octapharma Pharmazeutika Produktionges.m.b.H.
Oberlaaer Strabe 235, A-1100 Vienna
Austria

Octapharma AB
Elersvagen 40, SE-112 75 Stockholm
Sweden

Manufacturer of the medical device

NidaCon International AB
Flöjelbergsgatan 16B
SE-431 37 Mölndal
Sweden

In accordance with Council Directive 93/42/EEC, as amended, a sample from each batch of bulk and/or finished product of the human blood derivative shall be tested by a state laboratory or a laboratory designated for that purpose by a member state.

1.3. Recommended measures to the notified body

As discussed at CHMP, it would be recommended that the notified body request the following from the medical device manufacturer for device approval:

Area[1]	**Description**
Quality	Although data suggests that the proposed new test method for albumin concentration is acceptable for its purpose to determine the albumin concentration in in-process samples and final product testing of PureSperm Wash, no validation report has been provided. The notified body is strongly recommended to request the manufacturer of the medical device to initiate a validation study to confirm that the test is suitable to determine the Human Albumin concentration in PureSperm Wash.

[1] Areas: quality, safety, including clinical benefit/risk profile.

2. Scientific overview and discussion

2.1. General information

PureSperm Wash is classified as a class III medical device according to the Council Directive 93/42/EEC. The Notified Body, Det Norske Veritas Certification AS, is consulting the CHMP for a scientific opinion in accordance with Directive 93/42/EEC, as amended, regarding the quality and safety including clinical benefit/risk of the albumin component of PureSperm Wash.

PureSperm Wash is a sterile isotonic salt solution that contains human serum albumin (HSA). PureSperm Wash is used for In Vitro Fertilisation (IVF) and Assisted Reproductive Technologies (ART).

PureSperm Wash is to be used to extend the ejaculate prior to an intrauterine insemination (IUI), to wash a sperm pellet recovered from a PureSperm density gradient and for in vitro storage of sperm. It can also be used in the swim-up preparation.

About the ancillary medicinal substance

PureSperm Wash uses Albunorm 250 g/l manufactured by Octapharma as albumin source, which is a Human Albumin Solution 25%. The final product is marketed in some EU member states and meets the requirements of Ph. Eur. Monograph 'Albumin human solution'.

Table: Composition of Human Albumin Solution 25%

Name of Active ingredients	**Quantity**	**Function**
Plasma proteins with at least 96% human albumin	250g per 1000mL	Active ingredients
Name of Excipients	**Quantity**	**Function**
Sodium		Osmotic and electrolytic component
N-acetyl-DL-tryptophan		Stabiliser
Caprylic acid		Stabiliser
Water for injections		Solvent
Name of other components	**Quantity**	**Function**
Potassium		Osmotic and electrolytic component

About the medical device

PureSperm Wash is a sterile isotonic salt solution that contains human serum albumin (HSA). The amount of human serum albumin in PureSperm Wash is 5.65 g/l. There is no manipulation of the albumin before adding it to the medical device solution.

The principal reason for including HSA in the product is to avoid the sperm from sticking to the glass or plastic tubes (adhesion) or to each other (aggregation). This is feasible because albumin is strongly negatively charged.

PureSperm Wash is used for an intrauterine insemination treatment, the route of administration can be considered intrauterine since the prepared sperm are transferred into the uterine cavity suspended in the fluid PureSperm Wash. All other applications with this product involve in vitro cell maintenance.

2.2. Quality documentation

2.2.1. For the ancillary medicinal substance or the ancillary human blood derivative itself

In the initial application form and its annexes it was stated that Albunorm 250 g/l, which has been approved in several EU countries in a decentralised procedure, is used as albumin in the medical device PureSperm Wash. For the plasma, reference is made to Octapharma's PMF which has been certified in the centralised PMF procedure.

In the initial application, the information provided in section 3 of the PureSperm Wash dossier was not fully in accordance with Ph. Eur. requirements and with the marketing authorisation dossier of Albunorm approved in EU. A number of major objections were raised at Day 120 and the applicant was

asked to clearly state which albumin was delivered to NidaCon International AB by Octapharma and to update module 3 and the information regarding the plasma used accordingly.

In the response to Day 120 LoQ, Octapharma confirmed that it is the Albunorm 250 g/l manufactured and tested in accordance with the product approved in EU which is delivered for use in PureSperm Wash. A revised module 3 was provided. As a consequence most of the questions raised at Day 120 regarding the Albumin before incorporation were considered no longer relevant.

Drug substance

Starting material

The starting material for the manufacture of Human Albumin Solution 25% is human plasma.

Initially, there were conflicting information regarding the origin and quality of the plasma used. In the responses to day 120 LoQ, the applicant confirmed that the albumin used in PureSperm Wash is Albunorm 250 g/l in accordance with the EU approved product. It also clearly stated that all plasma used complies with the current version of Octapharma's Plasma master file (PMF). An EMA certificate of compliance (EMEA/H/PMF/000008/05/AU/009) dated 15 March 2012 was provided.

A letter of confirmation has been provided by the PMF holder to notify the medical device manufacturer, NidaCon International AB, in case of modification to the PMF or product recalls due to look back procedures.

Manufacture, Specifications, Stability

The applicant submitted all the details regarding the manufacture, specifications and stability of human albumin as active substance under the Drug Product section. Therefore this information can be found in the drug product section.

Drug product

Human Albumin Solution 25% is a solution for infusion, used for intravenous administration. The product is filled in infusion bottles containing 50mL and 100mL. The bottles are closed with bromobutyl rubber stoppers.

The qualitative and quantitative composition is detailed in section 2.1. - General information.

Pharmaceutical development

The manufacturing process of human albumin is based on various modifications to the well-established Cohn Oncley process to obtain better recoveries of albumin. Standard stabilisers are added to limit the potential degradation of high temperature pasteurization. The final formulation specifications are in accordance with European Pharmacopoeia.

The compatibility between the product and the container was demonstrated in stability studies. A study to demonstrate the integrity of the container closure system to prevent microbial contamination was provided.

Manufacturers

Human albumin solution 25% is manufactured from the starting material (human plasma pools) up to the finished product at two manufacturing sites, Octapharma Pharmazeutica Produktionsges.m.b.H, Vienna, Austria and Octapharma AB, Stockholm, Sweden.

Manufacturing licences issued by an EU Competent Authority have been provided.

Manufacturing process

The albumin described in module 3 is manufactured according to the principles of the Cohn fractionation.

The solution is filtered and may be stored in stainless steel tanks or single use bags.

The production of the finished product consists of sterilizing filtration and aseptic filling into the final container, pasteurization and incubation in the final container.

The manufacturing process, together with the validation data from both manufacturing sites has been described in sufficient detail. The processes at the two sites seem to be very similar with the exception of the optional steps. This is acceptable.

Process validation and batch data have demonstrated consistency of the manufacturing processes, with reduction of impurities to low levels. The final product complies with the Ph.Eur. monograph for human albumin solution (01/2010:0255).

The composition and physicochemical properties of intermediate fractions have been extensively studied. The manufacturing process is controlled by adequate in-process testing in all critical steps throughout the process. The test methods have been validated and adequate acceptance criteria established. All excipients are of pharmacopoeial grade (Ph.Eur).

Specifications

The drug product specification for Albunorm 250 g/l fulfils the requirements in the European Pharmacopoeia (Ph. Eur.) monograph 0255. Detailed descriptions of each analytical procedure and the corresponding validations are provided as well as the reports concerning method comparison or method transfer.

Container Closure system

The albumin is filled into 70 mL (filing volume 50 mL) and 100 mL bottles. The glass bottles are closed with bromobutyl rubber stoppers and sealed with flip-off caps. Details of suppliers have been given.

Stability

The stability results obtained prove compliance with the drug product specifications and have demonstrated that the final product, human albumin solution 25% can be stored at +2°C to +25°C, protected from light.

Adventitious agents' safety

TSE safety

No materials of bovine or other TSE-susceptible animal species are used for the production of Human Albumin Solution 25% from plasma to final product.

The capacity to remove prions has been assessed in accordance with the "Guideline on the investigation of manufacturing processes for plasma-derived medicinal products with regard to vCJD risk" (CPMP/BWP/5136/03). The studies performed are acceptable.

Viral safety

The viral safety of albumin is based on two steps. Both the studies for cold ethanol fractionation and pasteurisation were performed with appropriate in-process and final container material.

Effective reduction in two separate steps was demonstrated for HIV-1, PRV, Sindbis Virus (SBV). Octapharma has also provided a virus risk assessment. Satisfactory safety limits was demonstrated for

enveloped virus. Acceptable safety limit has also been presented for HAV. However, the data provided do not show any safety limit for parvovirus B19. Octapharma argues that the calculations are worst case calculation and for parvo B19, the much higher heat sensitivity documented for B19 compared to the one seen for PPV must be taken into consideration when these figures are evaluated. This is acceptable for albumin used for infusion since Albumin manufactured according to established manufacturing processes such as Cohn, has an excellent safety record with regards to virus transmission, when used in accordance with approved indications and route of administration

2.2.2. For the ancillary medicinal substance or the ancillary human blood derivative as incorporated in the medical device

Qualitative and Quantitative particular of the constituents

PureSperm Wash is a sterile isotonic salt solution containing physiological salts and 5.65 g/l of Human Serum Albumin added from Human Albumin Solution 25% manufactured by Octapharma. Pure Sperm Wash is used for rinsing or washing human sperm pellet after they have been purified, concentrated and recovered from a PureSperm density gradient. It can also be used in the swim-up method and for extending semen, or for transporting sperm pellet for use in IUI.

PureSperm Wash can be marketed in three different package sizes (5x) 6mL, (2x) 20 mL and (1 x) 100 mL.

Description of method of manufacture

Production of PureSperm Wash takes place in two facilities.

The manufacturing process has been described in sufficient detail. In general, the manufacturing process consists of the following steps: mixing of the ingredients, filtration and filling.

The manufacturer of the medical device has provided satisfactory data of stability of the Albumin.

Control of starting materials

Testing of starting material will be performed or not depending on manufacturing site. In any case, a thorough testing of the PureSperm Wash is performed as a part of the release process.

This approach was considered acceptable following confirmation that each batch of Human Albumin Solution 25% is manufactured by Octapharma in accordance with a valid EU marketing authorisation and has been subject to OMCL batch release. Furthermore, the applicant confirmed that Human Albumin Solution is stored according to the manufacturer's labelled conditions until used for incorporation in the medical device.

A batch record system allows the traceability of the human albumin solution used for every production of PureSperm Wash. It was confirmed that both Octapharma and NidaCon International AB stores the traceability data for 30 years in compliance with the requirements of Art 4 of Dir 2005/61/EC, Art 14 of Dir 2002/98/EC and GMP Annex 14.

Control test carried out at intermediate stages of the manufacturing process of the medical device

Initially, the device manufacturer claimed that no specific test at intermediate stages related to the incorporated human blood derivative was justified on the basis that the biological assay used at final control tests was considered sufficient to ensure accurate albumin concentration.

However, during the procedure the medical device manufacturer introduced a test for albumin concentration as an in process control, before the filtration step.

Final control tests of the ancillary medicinal substance or the ancillary human blood derivative in the medical device.

Initially there was no test for albumin content during production or at release of the final product. Such a test was requested as major objection at D120 LOQ and D180 LoOI. In the responses to D180 LoOI, the manufacturer of the medical device has introduced a test for Albumin concentration, both as in-process testing (before filtration) and in the final product testing of PureSperm Wash. The test is performed using a commercial kit. The description of the test method is provided but no proper validation report. However, data provided from testing of several batches of PureSperm Wash indicate that the test is suitable for its purpose.

All batches of PureSperm Wash undergo both quantitative tests and a qualitative test in the form of a biological assay on human ejaculates (both motility and viability are measured).

The biological assay used in release testing of PureSperm Wash is also claimed sufficient in detecting a change in protein content since the sperm would react to such changes. The manufacturer of the medical device has performed testing on different concentrations of human serum albumin and the effects on sperm are stated to be clear although no data has been provided.

Taking all this information together it can be accepted that no results from validation of the test method for Albumin has been provided although the manufacturer of the medical device is strongly recommended to initiate a validation study to confirm that the commercial test is indeed suitable to determine the Albumin concentration in PureSperm Wash. This aspect could be verified by the notified body.

Stability

PureSperm Wash can be stored in the bottle at room (ambient) temperature until opened. In this condition, the PureSperm Wash contents have a shelf-life of twelve months, i.e., from the production date to the expiry date.

A study was provided demonstrating that the biological performance of Pure Sperm Wash is unaffected during 11-month storage in a refrigerator with samples taken under aseptic condition numerous times. Additional data was also provided for batches which had been stored either at room temperature for the duration of the shelf-life, in the incubator 5 days at 50°C, in the freezer for 5 days. The visual control showed no evidence of visual aggregates in any of the samples and the albumin concentration was within the expected limits. This is an acceptable confirmation of product in-use stability with regards to the stability of albumin.

The human serum albumin used in the production is always within its shelf-life and will remain within its shelf-life throughout the duration of the shelf-life of the medical device PureSperm Wash.

Viral safety

Normally, a virus risk assessment is not required for Albumin used within the approved indications, but in this case the albumin is used for other purposes. Therefore, a virus risk assessment was requested for PureSperm Wash. Octapharma has provided a virus risk assessment in accordance with chapter 9 assessing the risk for virus transmission (former guideline CPMP/BWP/5180/03) of Guideline on plasma-derived medicinal products (EMA/CHMP/BWP/706271/2010) for the Albumin itself (see section 2.2.1. Adventitious Agents safety).

Although the manufacturer of the medical device has not performed a virus risk assessment with regards to parvo B19 for PureSperm Wash, the company provided enough information to enable a

further risk calculation by the assessor which concluded that the estimated virus particles “per dose” would be 0.9 IU. Since this is based on a worst case calculation, the risk of parvo B19 transmission is considered negligible.

2.2.3. Discussion and conclusion on chemical, pharmaceutical and biological aspects

For the Albumin itself

The manufacturer of the albumin, Octapharma, has confirmed that the albumin solution to be used in the manufacture of PureSperm Wash is in fact the same Albunorm product as licensed for use in the EU and therefore the points raised in relation to the quality of the human blood derivative itself is considered resolved. A new module 3 for Albunorm 250 g/l approved in EU has also been provided. It is also clearly stated that all plasma used comply with Octapharma’s PMF EMEA/H/PMF/000008/05/AU/009 and are in accordance with current requirements. Details of the pharmaceutical grade albumin have been provided, demonstrating a consistent product suitable for use as an ancillary medicinal product.

Safety of the human albumin has been assured by a combination of the EMA PMF, in-process controls and QC release testing for the manufacturing of Albumin 25%, capacity of the manufacturing process for viral reduction/inactivation and potential prion reduction studies, and official release by an OMCL.

Albumin after incorporation into medical device

The major objection raised regarding the virus safety of PureSperm Wash has been resolved.

Although the manufacturer of the medical device has not performed a virus risk assessment with regards to parvo B19 for PureSperm Wash as requested, the company provided enough information to enable a further risk calculation by the assessor which concluded that the estimated virus particles “per dose” would be 0.9 IU. Since this is based on a worst case calculation, the risk of parvo B19 transmission is considered negligible.

The manufacturer has also provided enough data to ensure the quality and safety of the Albumin. A test for albumin was introduced both as in-process testing (before filtration) and in the final product testing of PureSperm Wash to ensure the quality of albumin at release of the media.

2.3. Non-clinical documentation

Pharmacodynamics

Physiological/biochemical salt solution is used for sperm transport to the uterine cavity for intrauterine insemination and sperm survival during preparation for ART (assisted reproductive technology).

The medical device in question is used for rinsing or washing human sperm after it has been purified and concentrated on a density gradient. This washing process is done in either a glass or more often a plastic test tube, and the surfaces of these tubes have an electrical charge and may also have hydrophobic effects. The sperm cells being washed all carry a negative charge on their cell surfaces, while also the albumin molecule itself has strong negative charge. The resulting attraction and repulsion effects stop the sperm cells from sticking to the glass or plastic test tube (adhesion), or to each other (aggregation). This is the principal reason for including albumin in the product.

HSA accounts qualitatively for more than half of the total protein in the plasma and represents about 10% of the protein synthesis activity in the liver. The most important physiological functions of human albumin results from its contribution to oncotic pressure of the blood and transport function. Albumin

stabilizes circulating blood volume and is a carrier of hormones, enzymes, medicinal products and toxins.

Pharmacokinetics

No pharmacokinetics studies were submitted by the applicant. The applicant stated that pharmacokinetics for PureSperm Wash is not applicable since all the components are physiological except for EDTA. EDTA can be found to be used in, for example food as a preservative or in cosmetics to improve their stability toward air.

PureSperm Wash is not administered to patients when used for the washing procedure but is administered intra uterine when used for insemination. The amount of PureSperm Wash transferred into the reproductive tract in an IUI is 0.5 ml. PureSperm Wash contains a concentration of Human Albumin Solution 25% of 5.65 g/l. By increasing the safety margin and assuming the amount administered to 1 ml, a woman of 60 kg would receive a concentration of 0.1 g/kg of Human Albumin Solution 25%. It is assumed that this amount would dissipate in this luminal mucus environment within hours. The female genital tract will be locally exposed to PureSperm Wash containing human albumin and therefore, in response to the CHMP Day 120 List of Questions, a discussion has been provided in line with the "Guidance on the documentation to be provided by the notified body to the competent authority as given in the medical devices Guidance Document MEDDEV 2.1/3 rev 3, Section C".

Toxicity

No non-clinical toxicology studies with Human Albumin Solution 25% have been conducted. Human Albumin is a normal constituent of human plasma and acts like physiological albumin. No non-clinical toxicology studies have been conducted with PureSperm Wash since the product contains no components with known toxicological effects.

Summaries of two pre-clinical studies were submitted by the applicant. The quality of the sperms regarding numbers, morphology and motility after retrieval from a standard density-gradient separation from semen, and followed by a washing step in PureSperm were studied and compared to a well-established washing medium (Quinn's Washing medium). No differences were seen in terms of sperm number or morphology. At CHMP request, the exact composition of Quinn's Washing Media and its validity for its use as a comparator in the pre-clinical studies has been further explained.

Local tolerance

The applicant has not presented any studies to address the local tolerance of PureSperm Wash. The applicant argues that since the amount of human albumin administered in the female reproductive tract is small and will dissipate within hours, no local tolerance studies are required. PureSperm Wash is administered in the female genital tract during intra-uterine injection of semen. In response to the CHMP Day 120 List of Questions, information on local tolerance regarding irritancy and sensitising potential of the ancillary human blood derivative was provided by the applicant.

2.3.1. Discussion and conclusion on the non-clinical documentation

Human serum albumin is a constituent of normal blood which is a well-known substance used in IVFmedia for over 20 years. Historically, media have been supplemented with protein in the form of either serum albumin or serum. The role of albumin in media used for ART includes colloid osmotic regulation and as a coating agent to prevent the attachment of cells to laboratory ware.

The lack of pharmacokinetic studies is acceptable since the proposed reproductive media solutions are not expected to cause any systemic exposure to the ancillary human blood derivative in the patient.

The applicant`s justification for not submitting toxicology data was accepted and the inclusion of albumin did not raise a concern regarding local tolerance.

There are no objections from a non-clinical point of view to acceptance of the proposed ancillary substance used in the medical device, PureSperm Wash.

2.4. Clinical evaluation

2.4.1. Usefulness of the ancillary medicinal substance incorporated in the medical device as verified by notified body

The medical device manufacturer has submitted a brief critical review. Furthermore, the results from two comparative clinical studies are presented.

The Notified Body has assessed and verified the design dossier and the technical file for the NidaCon International AB medical device PureSperm Wash as well as the different production steps with the focus on the usefulness of human serum albumin.

The review of clinical evaluation was found adequate and the role of human serum albumin in ART for sperm preparation is considered well established. In the clinical studies, the NidaCon - and Vitrolife media were comparable regarding the pregnancy rate.

2.4.2. Clinical safety of the ancillary medicinal substance incorporated in the medical device

The possible risk of transmitting infections with human serum albumin in ART is well outlined, and considered low, and the clinical safety associated with the addition of albumin to the medical device is considered as acceptable.

2.4.3. Clinical benefit/risk profile of the ancillary medicinal substance incorporated in the medical device

The discussions provided by both the medical device manufacturer and Notified body on albumin's physiological roles and the established use of human serum albumin supplementation of ART media, in addition to the literature evidence provided by the medical device manufacturer, together sufficiently demonstrated the usefulness of human serum albumin added to the ART media. Further, the applicant has outlined the well-established safety profile of human albumin and has clearly detailed the risks of human albumin, particularly the risk of transmissible infections, which are generally considered to be low.

The clinical risk benefit balance can be considered to be favourable.

2.4.4. Discussion and conclusion on the clinical evaluation

The established practice of human serum albumin supplementation of ART media is well recognised and widely accepted. The medical device manufacturer has submitted published literature and clinical studies to demonstrate the usefulness of human serum albumin supplementation of ART media for sperm preparation. Taken together, the literature submitted and record of clinical studies sufficiently demonstrated the usefulness of Human Albumin Solution 25% added to ART media for sperm preparation.

The medical device manufacturer outlined the well-established safety profile of human albumin and has clearly detailed the risks of human albumin used within these media, particularly the risk of transmissible infections.

2.5. Overall conclusions

Satisfactory quality and safety has been demonstrated for the Human Albumin Solution before incorporation into the medical device. Manufacture and control of the human albumin has been adequately described. All questions raised have also been satisfactorily addressed.

With regards to Human Albumin Solution after incorporation in the medical device, the applicant has demonstrated the maintenance of the quality of human albumin in the medical device.

The clinical benefit-risk balance of the ancillary medicinal substance albumin in the context of its use in the medical device is considered to be positive.

2.6. Recommendation

Based on the CHMP review of data submitted, the CHMP considered by consensus that the quality and safety including the benefit risk profile of Human Albumin Solution used as ancillary medicinal substance in the Pure Sperm Wash was favourable and therefore granted a positive opinion in the consultation procedure.