ELECTROSTATIC PRECIPITATION OF LAPAROSCOPIC SURGICAL SMOKE BY THE ULTRAVISION™ SYSTEM

The Ultravision™ system removes smoke and particulate matter produced during electrosurgical procedures, as an aid to maintaining a clear visual field. It does so by the electrostatic precipitation of particulate matter generated within the peritoneal cavity.

Non-clinical and clinical studies, including extensive experience in patients following exposure to intraperitoneal surgical smoke, have demonstrated the safety of the Ultravision™ system and confirmed that there is no evidence of significant risk associated with volatile, partly volatile or particulate components of surgical smoke being retained within the peritoneal cavity.

The performance and safety of the Ultravision™ system as claimed by the manufacturer have been demonstrated.

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Abbreviations Used:

CEBM Centre for Evidence Based Medicine; FDA Food and Drug Administration; GLP Good Laboratory Practice; MHRA Medicines and Healthcare products Regulatory Agency; PRISMA Preferred Reporting Items for Systematic Review and Meta-Analyses;

Surgical smoke is a collective term for the particulate and volatile matter generated as a result of tissue resection using energy-based surgical instruments. Particulate size is determined by the type of energy used. Electrosurgery generates particulates with the smallest mean aerodynamic size, 0.07um[1,2]; laser tissue ablation creates particulates with a mean size of 0.31um[3]; ultrasonic devices generate the largest particulates, with a mean size 0.35-6.50um[3,4].

The volume and composition of smoke can vary widely between different surgical procedures, depending on procedure; tissue pathology; type of energy and the power at which it is delivered; surgical technique; and the amounts of cutting, coagulation or ablation involved[5,6]. The effects of using different energy based surgical devices on both smoke production and laparoscopic visibility have only been recently quantified[7].

In an effort to fully define and quantitate the hazards to health (both real and potential) that are posed by surgical smoke exposure, its chemical composition, biological properties and health impact (for both patients and healthcare professionals) have been investigated and reported by a multitude of authors[6-22].

During laparoscopic surgery, surgical smoke obscures the surgeon's field of vision. When smoke is present to a level that prevents surgery continuing, current Standard of Care is to either simply halt the procedure and wait for the smoke to clear, or to open a valve on one of the surgical ports and actively release it into the operating theatre environment. An alternative option is the use of a system that actively removes the smoke. Currently marketed systems predominantly utilise vacuum filtering as their mode of action. However, their use is very limited and feedback from surgeons and other users has been described as "universally negative"[23].

The particulate removal capability of approved vacuum smoke evacuator devices is, by design, limited by the size of the aperture through which smoke is removed and by the efficiency and size of their filters; typically 99% for particulates above 100nm. Particles smaller than 100nm are not retained and therefore enter the operating theatre environment.

The Ultravision™ system removes smoke and particulate matter produced during electrosurgical procedures by electrostatic precipitation onto the surfaces of the peritoneal cavity. Functionality is not restricted by particle

size and >99% of all smoke particulates >7nm in size are removed. It is therefore essential to demonstrate that the deposition and retention of the components of surgical smoke does not present a risk to the patient. Alesi has achieved this by a combination of approaches, which are listed below and detailed in this summary review.

1. Independent expert reviews of the literature
2. Independent expert toxicological report
3. Pre-clinical testing and evaluation
4. Clinical evaluation in human subjects

Expert Reviews

In addition to pre-clinical and clinical assessments evaluations, Alesi has commissioned a number of independent reviews to support product registration and safety. These reviews, of the clinical literature and toxicological implications of retaining surgical smoke within the peritoneal cavity, are summarised below.

Literature Reviews

A review of the published clinical literature and international Adverse Event databases was undertaken in 2011[24] and updated in 2013[25]. Clinical and scientific literature, clinical trials databases, government data sources and the websites of healthcare professional bodies were searched using recognised methodologies and keywords to identify appropriate sources of information.

Neither review identified any evidence to contra-indicate the use of the Ultravision™ system for its intended purpose. Furthermore, the clinical and scientific literature endorsed the approach to the management of surgical smoke implemented by the Ultravision™ system.

Systematic Review

A systematic review of the published literature investigating the hazards of surgical smoke was conducted in 2013[26]. This was the first, and to date remains the only, such review in this area to have been undertaken following PRISMA guidelines[27]. Searches of MEDLINE, PubMed, Cochrane database, Embase classic + Embase, and the metaRegister of controlled trials for studies detailing the evaluation and effects of surgical smoke were performed independently by two reviewers.

Studies were included if they documented the constituents found in surgical smoke during human surgical procedures, the methods used to analyse the smoke, the implications of exposure to smoke, and the type of energy-based surgical instrument that generated the smoke. Only original articles were included. Studies were excluded if they were animal based, pre-clinical experimental work, conference abstracts, or opinion-based reports. Included studies were rated according to CEBM guidelines[28]. Each paper was examined to identify the energy device used, the smoke properties and particle size, the risk of infection, and the mutagenic risk. Additional materials, including manual searches and information from specialist textbooks, government agency publications, and healthcare professional organisations, were used to prepare the background information for the review. Common end points between studies were identified and compared. Data from studies with a heterogeneous design were judged not suitable for meta-analysis.

The authors of the review concluded that whilst potential for harm from surgical smoke exists, there is little evidence for long-term effects of surgical smoke *in vivo* and the risk presented to operating theatre staff remains unproven.

Summary: Expert Reviews

Two comprehensive literature reviews and a systematic review have been unable to identify any evidence that a single, acute dose exposure to surgical smoke during laparoscopic surgery represents any significant hazard to the patient. This conclusion is further supported by the absence of any reported Adverse Events in FDA databases, despite the ~2.5m laparoscopic procedures performed each year[24,25].

Toxicology Report

In order to further evaluate the potential risks to the patient an independent toxicological report[29] examined the potential hazards and risks of an acute dose exposure to surgical smoke in the following areas:

- Local acute tolerance;
- Systemic acute tolerance;
- Local chronic tolerance;
- Distributed chronic toxicity;
- Distributed and local carcinogenicity and mutagenicity.

Potential toxic components of smoke generated by combustion of tissue in a CO_2 environment, during laparoscopic surgery, were identified by a detailed search and review of the literature. A quantitative risk assessment was performed, comparing and contrasting the risk from procedures of limited duration or with minimal tissue cutting, to more extensive procedures. A worst case scenario approach was adopted throughout. Where possible, assessment was carried out in comparison with available reference values, to establish expected safe levels relevant to any identified hazards.

Summary: Toxicology Report

The toxicology report concluded that non-clinical and clinical studies, including extensive experience in patients following exposure to intraperitoneal surgical smoke, have demonstrated the safety of the Ultravision™ system and confirmed that there is no evidence of significant risk associated with volatile, partly volatile or particulate components of surgical smoke being retained within the peritoneal cavity.

Pre-clinical safety evaluation

Pre-clinical safety was evaluated in an independent GLP study[30] conducted with monopolar, bipolar and harmonic electrosurgical devices in a 28 day porcine

recovery model. The objective of the study was to demonstrate that retention within the peritoneal cavity of all the surgical smoke resulting from the use of the three different types of devices was safe. Six animals, each weighing ~40kg, were used.

Monopolar and bipolar devices were used in three animals and a harmonic device used in the remaining animals.

Device use was identical to that adopted in routine human surgery, but the duration of tissue cutting was adjusted to the weight of the animal and increased to approximately 1.5-fold that of normal surgery in humans. This provided, on a dose/kg basis, approximately 1.5-fold the expected dose of surgical smoke for an equivalent 60kg human patient.

Vital signs, blood gases, haematology and clinical chemistry were evaluated pre-operatively, immediately post-operatively and again following euthanasia 28 days later. A range of relevant tissues (from the peritoneal wall, mesenteric lymph nodes, abdominal organs and cardiovascular system) were evaluated histologically (3 sections/site, n=240) by an independent pathologist blind to both the experimental animal from which the tissue was sourced and the type of electrosurgical device used.

Examination highlighted no pathological findings of note at either macroscopic or microscopic levels.

Clinical chemistry, haematology and cellular histology were normal in all cases, even where post-operative lavage of the abdomen had not been undertaken.

Summary: Pre-clinical Evaluation

The pre-clinical evaluation conclusively demonstrated a total absence of any detrimental observations which could be linked to the application or use of the Ultravision™ system.

Clinical evaluation

Following approval from the UK Competent Authority, MHRA, a single centre, prospective, randomised clinical trial evaluating Ultravision™ was undertaken in a population of thirty patients undergoing elective laparoscopic cholecystectomy for documented symptomatic gallbladder disease[31,32]. Study participants were randomised in a 1:1 ratio to either Ultravision™ "on" or "off" during surgery. Primary objectives of the study were safety and performance. Safety was evaluated by incidence of adverse events and measuring levels of CO and MetHb in the patients' bloodstreams before and after their surgery.

Summary: Clinical Evaluation

The clinical evaluation confirmed that the Ultravision™ is safe to use in the operating theatre. There were no adverse events during the study and there was no detectable difference in either CO or MetHb levels between the two groups of patients pre- and post-surgery. The median change in baseline levels of CO in both groups was 0%.

Conclusion

Commensurate with the available evidence, and independent expert opinion, the Ultravision™ system can be considered safe and effective for its intended use.

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