Clinical Evaluation Summary Report Examination Gloves

Latex Powdered (non-sterile)
Latex Powder Free (non-sterile)
Nitrile Powder Free (non-sterile)

Revision 3.0

Manufacturer:

Sri Trang Gloves (Thailand) Public Company Limited
10 Soi 10, Phetkasem Road,
Hat Yai, Songkhla 90110, Thailand

Revision 3.0

Number of Version	Changes performed
Version 1.0 (24.09.2015)	New document for non-sterile latex and nitrile examination gloves
Version 2.0 (18.09.2017)	Adjustment to the requirements of the MEDDEV 2.7.1/ Rev.4
Version 3.0 (07.09.2020)	Adjustments to the requirements of the MDR 2017/745, parts of the clinical evaluation report were included in the required clinical evaluation plan revision 0.0

1. Scope of the Clinical Evaluation

1.1. Device identification

The clinical evaluation was written for the group of non-sterile examination gloves with the same intended purpose and user. In general, the document covers non-sterile examination gloves made of latex powdered, latex powder free and nitrile - powder free. Additionally, two nitrile glove products are free from accelerators, which will be an additional issue covered by the literature search. The following table presents the details of the different examination gloves in more detail. The different models are covered by the respective Declaration of conformity (valid until 2025-05-18). Generally, the gloves are available in different sizes that allow the user to choose the best fitting size (sizes: XS, S, M, L, XL). The main differences between the products are displayed in table 1. More details about the product configuration are available in the technical file. The gloves are sold in a dispenser box with labelling according to MDR. No relevant changes in regards to design change, changes to materials and manufacturing procedures, changes to the information materials like labeling, IFU or promotional materials and to other claims have been introduced since the last version of the clinical evaluation, revision 2.0.

Table 1: Overview of the products under evaluation and their main differences.

Product code	Material	Method of chlorination	Powdered?	Accelerator?	Available colors
LC01	latex	offline	free	Yes	white
LO01	latex	online	free	Yes	pale yellow, color may vary due to storage time and condition
LX01	latex		yes	Yes	white
NC01	nitrile	offline	free	Yes	white, pink, blue, violet blue, black, ocean blue
NC02	nitrile	offline	free	Free	violet blue
NO01	nitrile	online	free	Yes	blue
NO02	nitrile	online	free	Yes	violet blue, black, dark ocean blue, ocean blue, white, dark blue
NO03	nitrile	online	free	Free	violet blue, white, black
NO04	nitrile	online	free	Yes	violet blue, white, ocean blue

1.2. Legal manufacturer

The legal manufacturer according to EU Regulation 2017/745 is:

Sri Trang Gloves (Thailand) Public Company Limited

10 Soi 10, Phetkasem Road, Hat Yai, Songkhla 90110 Thailand

The manufacturing facilities are the following:

Site 1 (STGT-HY1): 110 Kanjanavanit Road, Pahtong, Hat Yai, Songkhla 90230 Thailand

Site 2 (STGT-HY2): 109/2Kanjanavanit Road, Pahtong, Hat Yai, Songkhla 90230 Thailand

Site 3 (STGT-HY3): 352 Kanjanavanit Road, Pahtong, Hat Yai, Songkhla 90230 Thailand

Site 4 (STGT-HY4): 110/3 Kanjanavanit Road, Pahtong, Hat Yai, Songkhla 90230 Thailand

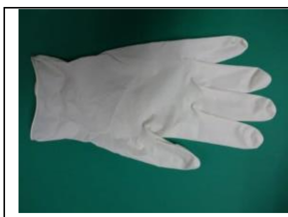
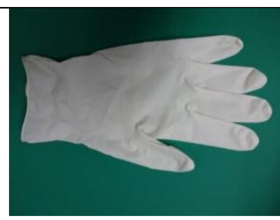
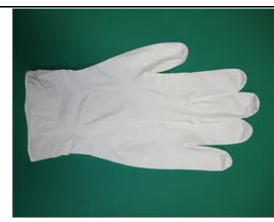
Site 5 (STGT-SR): 189 Moo 7, Phlai Wat, Kanchanadit, Surat Thani 84160 Thailand

Site 6 (STGT-TG): 85 Moo 6, Kuan Thani, Kantang, Trang 92110 Thailand

The clinical evaluation is performed according to the MDR and in principal structured according to current MEDDEV 2.7/1 revision 4.

1.3. Product description

The non-sterile examination gloves (latex powdered, latex powder free and nitrile - powder free) are disposable gloves used during medical examinations and procedures that help prevent contamination between examiner and patients (representative pictures are shown in figure 1, 2 and 3).

 *Figure 1: Latex examination glove, powder free, non-sterile* *(example from technical file of product LC01)*	 *Figure 2: Latex examination glove, powdered, non-sterile*	 *Figure 3: Nitrile examination glove, powder free, non-sterile* *(example from technical file of product NC01 (color white)*

The device under evaluation are made of latex or nitrile rubber. They are produced unpowdered (latex and nitrile) or powdered (latex) with USP-grade modified cornstarch to lubricate the gloves, making them easier to put on the hands. To compensate for the lack of powder, the unpowdered examination gloves (latex and nitrile) are either subjected to online- or offline chlorination. In general, online chlorination is a finishing method for powder free gloves. Here, the gloves are washed in a chlorine solution that reduces the surface tackiness of the glove and gives it a softer texture allowing gloves to be easily donned. When used on latex, the chlorination process also reduces the amount of latex proteins, to make them less likely to cause an allergy. For the offline chlorination process, the glove surface is in addition siliconized and the inside is coated with a synthetically material.

During the clinical evaluation, special attention is given to the applied materials that may cause skin sensitization or allergies. Additionally, data will be identified that cover the present or absence

of accelerators in gloves. Where applicable, the device under evaluation contains dithiocarbamate as accelerator. The accelerator is responsible for many characteristics of the glove but some of them might lead to contact allergies. Furthermore, the nitrile gloves are available in different colors, which will be also considered during this clinical evaluation. The table below shows the materials that are used during product manufacturing.

Table 2: Specifications of the device under evaluation.

Material/ Component	Function	Product code								
		LC01	LO01	LX01	NC01	NC02	NO01	NO02	NO03	NO04
Natural rubber latex	Main raw material	x	x	x	--	--	--	--	--	--
Sulphur	Vulcanizing agent	x	x	x	x	--	x	x	--	x
Dithiocarbamate	Accelerator	x	x	x	x	--	x	x	--	x
Polymeric sterically hindered phenol	Antioxidant	x	x	x	x	x	x	x	x	x
Zinc oxide	Activator	x	x	x	x	x	x	x		x
Titanium dioxide	Pigment	x	x	--	x	x	x	x	x	x
Potassium hydroxide	Stabilizer	x	x	x	--	--	x	x		x
Calcium Carbonate	Additive	x	x	x	--	--	--	--	--	--
Polyacrylic for latex	Coating	x	--	--	--	--	--	--	--	--
Cornstarch powder	Donning	--	--	x	--	--	--	--	--	--
Nitrile butadiene rubber (NBR) latex	Main raw material	--	--	--	x	x	x	x	x	x
Ammonium hydroxide	Stabilizer	--	--	--	x	x			x	
Polyacrylate for NBR	Coating	--	--	--	x	x	--	--	--	--
Pigment color	Pigment	--	--	--	x	x	x	x	x	x
Water based crosslinker	Vulcanizing agent	--	--	--	--	x	--	--	x	--

1.4. Intended use for non-sterile examination gloves:

As indicated by the manufacturer, a patient examination glove is a disposable device intended for medical purposes that is worn on the examiners hand or finger to prevent contamination between patient and examiner. The non-sterile examination gloves (latex powdered, latex powder free and nitrile - powder free) are intended for medical activities except surgery.

1.5. Claims on clinical performance and clinical safety foreseen by the manufacturer:

In the course of this clinical evaluation, claims that go beyond the intended use for the non-sterile powdered and powder-free latex examination gloves as well as for the powder-free nitrile examination gloves were not taken into consideration. Proof of those characteristics has to be done separately.

The claims that are raised in regards to the clinical performance and clinical safety by the manufacturer of the non-sterile examination gloves are the following:

- Latex powder free: comfortable touch, without leaving any residue, smooth easy donning for inner surface finish
  Source: homepage https://www.sritranggloves.com/en/our-business/products/latex-powder-free-examination-gloves (2020-04-20; 15:42)
- Nitrile powder free: rigorous sourcing and testing to ensure that nitrile from suppliers is up to STGT standards
  Source: homepage: https://www.sritranggloves.com/en/our-business/products/nitrile-powder-free-examination-gloves (2020-05-15; 11:10)

1.6. Achievement of intended purpose and underlying technology

Prevention of contamination between examiner and patient is achieved by a barrier worn on the examiners hand or finger based on natural rubber latex or nitrile latex, respectively. The non-sterile examination gloves are sold in the European Union since 1989 and the underlying technology has not changed since then. As described, chlorination will be applied to the gloves that will come unpowdered. The following technologies, called online- or offline chlorination are applied by the manufacturer to achieve this goal:

Offline – Chlorination:	Online – Chlorination:
• Halogenation / siliconization and extensive washing in water. Inside coated with synthetically material. Off-line-finish.	Halogenation and extensive washing in water online

1.7. Classification of the Medical Device

The non-sterile examination gloves (latex powdered, latex powder free and nitrile - powder free) are medical device, class:

I ☒ I_m ☐ I_s ☐ IIa ☐ IIb ☐ III ☐

According to the manufacturer the product is classified in accordance with rule 1 and rule 5 of annex VIII chapter III (classification rules), of the MDR 2017/745:

Rule 1:

All non-invasive devices are classified as class I, unless one of the rules set out hereinafter applies.

Rule 5:

All invasive devices with respect to body orifices, other than surgically invasive devices, which are not intended for connection to an active device or which are intended for connection to a class I active device are classified as:

— class I if they are intended for transient use;

The second and third indent of rule 5 are not applicable:

— class IIa if they are intended for short-term use, except if they are used in the oral cavity as far as the pharynx, in an ear canal up to the ear drum or in the nasal cavity, in which case they are classified as class I; and

— class IIb if they are intended for long-term use, except if they are used in the oral cavity as far as the pharynx, in an ear canal up to the ear drum or in the nasal cavity and are not liable to be absorbed by the mucous membrane, in which case they are classified as class IIa.

All invasive devices with respect to body orifices, other than surgically invasive devices, intended for connection to a class IIa, class IIb or class III active device, are classified as class IIa.

However, MDR 2017/745 Annex VIII sections 3.5. and 4.1. state,

"If several rules, or if, within the same rule, several sub-rules, apply to the same device based on the device's intended purpose, the strictest rule and sub-rule resulting in the higher classification shall apply."

"All non-invasive devices are classified as class I, unless one of the rules set out hereinafter applies."

In order to assure conformity with MDR 2017/745, only Rule 5 applies to the device in question. This does not affect the classification to class I.

1.8. Regulatory status

The non-sterile examination gloves (latex powdered, latex powder free and nitrile - powder free) were put onto the European market in 1989 and have not been modified to date. The manufacturer provided DoCs (signed 18 May 2020) that self-declare that the examination gloves described here meet all provisions of the Medical Device Regulation (EU) 2017/745 and Personal Protective Equipment Regulation (EU) 2016/425.

2. Clinical Background, Current knowledge, State of the Art

2.1. SCImago Journal Rank of retrieved articles

In the course of the update of the clinical evaluation, newly identified literature was evaluated using the SCImago Journal Rank index. The SCImago Journal Rank is a publicly available portal (https://www.scimagojr.com/index.php) that includes the journals scientific indicators developed from the information contained in the Scopus database (Elsevier B.V.). These indicators can be used to assess and analyze scientific domains. Journals can be compared or analyzed separately. Journals can be grouped by subject area (27 major thematic areas), subject category (313 specific subject categories) or by country. Citation data is drawn from over 34,100 titles from more than 5,000 international publishers and country performance metrics from 239 countries worldwide. The scientific quality of the retrieved articles is thought to be suitable for the analysis.

Table 3: SCImago Journal Rank of the included literature.

Ranking (Quartile)	Journal/Country	SJR indicator (2019)	Affected literature
Q3	Journal of Postgraduate Medicine/ India	0.37	(1) (2)
	Eastern Mediterranean Health Journal/ Switzerland	0.28	(3)
	Asian Pacific Journal of Allergy and Immunology/ Thailand	0.34	(4)
Q2	Contact Dermatitis/ United Kingdom	0.65	(5) (6) (7) (8) (9)
Q1	BMC Infectious Disease/ United Kingdom	1.39	(10)
	Cochrane Database of Systematic reviews/ United Kingdom	1.29	(11)
	Infection Control and Hospital Epidemiology/ United Kingdom	1.56	(12)
	Anesthesia and Analgesia/ United States	1.41	(13)
	American Journal of Infection Control/ United States	0.99	(14) (15)
	Dermatitis/ United States	1.35	(16) (17) (18)

Out of the presented table of SCImago Journal Rank, it is concluded that most of the articles that are retrieved by literature search are located in Q1 and Q2. Therefore, it can be assumed that the retrieved information from these publications is sufficient and adequate to show the clinical background, state of the art and current knowledge of the device in question. The identified literature, which presents studies related to the safety and performance of the device in question, is evaluated according the criteria that are described in the CEP, part 7.2.3, including the evaluation of the level of evidence. The evaluation is presented in the table below.

Reference	Medical product	Characteristics looked at	Relevant for	Amount of patients	Level of evidence	Weight of evidence	Tendency of the statement
(3)	*Latex examination gloves*	*Integrity of gloves and the longevity of their protective barrier function affected by longer finger nails*	*Safety and performance*	*User: 6*	*Level 6*	*D3* *A1* *P2* *R1* *S1* *L1*	*Indifferent*
(11)	*Any type of glove*	*Interventions for preventing occupational irritant hand dermatitis*	*Safety*	*--*	*Level 2*	*D3* *A3* *P1* *R3* *Not applicable* *L3*	*Indifferent*
(4)	*Powdered natural rubber latex (NRL) gloves*	*Determine amount of proteins and the effect of NRL gloves on the pulmonary function*	*Safety*	*Health care workers: 340*	*Level 7*	*Not indicated* *Not indicated* *P1* *R1* *S2* *L3*	*Unfavorable (for powdered examination gloves)*
(17)	*Examination gloves and surgical gloves*	*The goal was to ascertain the accelerators used in medical examination and surgical gloves.*	*Safety*	*190 gloves from 8 glove manufacturers within the USA*	*Level 7*	*D3* *Not applicable* *PNA* *R1*	*Indifferent*

						S1 *L1*	
(12)	*Nitrile gloves (Promed, Tanawha, Australia), latex gloves (Thermo Fisher Scientific, Scoresby, Australia) and sterile surgical gloves (Ansell Gammex PF DermaPrene Glove, Richmond, Australia)*	*Determination of the transmission of Staphylococcus aureus from dry surface biofilm via different types of gloves*	*Safety*	*3 glove types*	*Level 6*	*D3* *A1* *PNA* *R1* *S1* *L1*	*Indifferent*
(13)	*6.2 mil (Medichoice, XTS Nitrile exam gloves; Owens and Minor , Mechanicsville, VA)*	*Does the application of alcohol-based hand rub on examination glove influence glove integrity or hamper the ability to perform tasks.*	*Safety and Performance*	*1 glove type, 50 new gloves*	*Level 4*	*D3* *A1* *PNA* *R2* *S1* *L2*	*favorable*
(14)	*Survey of usage* *Latex gloves, powdered latex gloves and any gloves*	*Estimate the burden of asthma attributable to occupational exposure to latex among HCWs in Australia.*	*Safety*	*4878 people were called and asked*	*Level 7*	*D3* *A1, A2 and A3 possible* *P1, P2, P3 possible* *S1* *L2*	*Unfavorable (for latex examination gloves)*
(5)	*Ansell (Cammex Non-Latex Sensitive, Dermaprene, MICRO-TOTTCHii-accelerator-free)* ***and*** *Sempermed (Syntegra UV)*	*To assess the efficacy of accelerator-free medical gloves in the secondary prevention of allergic contact dermatitis caused by rubber accelerators in healthcareworkers.*	*Safety*	*9 HCWs*	*Level 5*	*D3* *A1, A2 and A3 possible* *P1* *R2*	*Favorable for accelerator-free examination gloves*

						S1 *L1*	
(15)	*Standard nitile examination glove and modified glove with a textured doffing aid above the thumb area for better donning (Doffy Gloves, IP gloves GmbH, Aachen, Germany)*	*Comparison of contamination rates with modified and standard glove*	*Safety*	*317 individuals*	*Level 2*	*D3* *A2* *P1* *R2* *S1* *L3*	*Unfavorable for non-modified gloves without doffing aid*
(6)	*Various gloves*	*To assess hand eczema and contact allergy related to occupational exposurein HCWs*	*Safety*	*425 HCWs*	*Level 3*	*D3* *A1, A2, A3 possible* *P1* *R1* *S1* *L1*	*Unfavorable for medical gloves with rubber additives*
(7)	*Protexis PI polyisoprene sterile surgical gloves, powder-free with a coating containing cetylpyridinium chloride (Cardinal Health, Waukigan, lllinois),* ***and*** *Sterling Nitrile non-sterile examination gloves (Kimberly-Clark, lrving, Texas)*	*To access whether skin exposure to rubber accelerator diphenylguanidine (DPG) released from glove materials is influenced by alcoholic hand disinfectans, time and pH*	*Safety*	*Up to 58 HCWs*	*Level 1*	*D3* *A1* *P1* *R1* *S1* *L1*	*Unfavorable for gloves with DPG*
(9)	*Glove containing diphenylguanidine and DGP free glove*	*Case report on relapsing polyisoprene glove allergic contact dermatitis*	*Safety*	*1 HCW*	*Level 5*	*D3* *A1, A2, A3 possible* *P1*	*Unfavorable for gloves containing rubber additives*

						R2 *S1* *L2*	
(8)	*The accelerator-free gloves: (a) Gammex Dermaprene (Ansell, Richmond, Australia), (b) Gammex Non-Latex Sensitive (Ansell),* *(c) Sempermed Syntegra UV (Semperit, Vienna, Austria), and (d) Neoderm biogel (NeoDerm, Gothenburg, Sweden)* *Esteem Micro and Ortho, and Sensicare lce Nitrile Exam Gloves; all of these are manufactured by Medline International. Sensicare lce Nitrile Exam Gloves contain dithiocarbamates but no DPG, whereas Esteem Micro and Ortho contain both dithiocarbamates and DPG.* *European baseline series: a rubber series, antiseptic and preservatives series (Chemotechnique Diagnostics, Vellinge, Sweden and SmartPractice, Reinbek, Germany), a sample series from gloves used by patients, and accelerator-free* *gloves.*	*Highlight the role of 1,3-diphenylguanidine as main allergen causing contact dermatitis after wearing rubber gloves*	*Safety*	*4068 patients were tested, 44 caregivers were included in the analysis*	*Level 3*	*D3* *A3* *P1* *R1* *A1* *L1*	*Unfavorable for gloves containing 1,3-diphenylguanidine*

2.2. Medical Background

Medical gloves were first introduced to surgical procedures more than a century ago, both for hygiene purposes and the prevention of hand dermatitis (19)(20)(11). Before that, in the nineteenth century - when medical gloves were not yet available, surgical hand preparation has been the most important measure to reduce infection resulting from surgery.

Historically, the connection between the transmission of germs and infections were first described in studies by Ignaz Semmelweis in Vienna, Austria and Oliver Wendell Holmes in Boston, USA. They established that hospital-acquired diseases were transmitted via the hands of health care workers (HCW). In 1847, Semmelweis was appointed as a house officer in one of the two obstetric clinics at the University of Vienna. He observed that maternal mortality rates, mostly attributable to puerperal fever, were substantially higher in one clinic compared with the other (18% versus 7%). He also noted that doctors and medical students often went directly to the delivery suite after performing autopsies and had a disagreeable odor on their hands despite hand washing with soap and water before entering the clinic. He hypothesized therefore that “cadaverous particles” were transmitted via the hands of doctors and students from the autopsy room to the delivery theatre and caused the puerperal fever. Therefore, Semmelweis required his students to wash their hands in an antiseptic disinfectant (chlorine) solution before examining patients. Following the implementation of this measure, the mortality rate fell dramatically from 18% to 1% in the clinic most affected and remained low thereafter (21)(20).

Later on in 1867, Joseph Lister, an English surgeon, published the groundbreaking paper “Antiseptic Principle of the Practice of Surgery” (20) while working at the Glasgow Royal Infirmary. He used 5% carbolic acid solution (or phenol) to spray instruments and wounds and made surgeons wash their hands before and after operations with this solution. In 1876, Lister traveled to the United States to present his ideas and impressed Dr. William Halsted with his findings. In 1884, Halsted returned to New York City after studying in Germany and refused to perform surgery in the old theater at Bellevue. Instead, he built a tent on the grounds of Bellevue that featured a gas stove to boil instruments. Halsted was sold on Listerian techniques, which were still somewhat controversial until German bacteriologist Robert Koch’s postulates in 1882 effectively proved that microorganisms caused disease (Koch later won the Nobel Prize in 1905). Subsequently in May 1889, Dr. William Halsted continued his work at Johns Hopkins University. Unfortunately, in the winter of 1889 and 1890, his scrub nurse developed a severe contact dermatitis, as her sensitive hands could not tolerate the disinfectants mercuric chloride and carbolic acid. As a consequence, Dr. Halsted asked the Goodyear Rubber Company to produce thin rubber gloves for her protection (20) and the first medical glove was born.

At the beginning of the 20th century, surgical gloves were reusable and had to be sterilized by boiling. Donning of the gloves however was only possible by pulling the rubber gloves over wet hands. Because of that, the wet hands of the surgical staff became macerated under the occlusive cover of the rubber gloves predisposing them to severe dermatitis. By the 1950s cornstarch powder became the lubricant on most surgical gloves, which facilitated donning (22). Subsequently in the 1960s, the first disposable gloves were developed. Throughout the 1990s there were increasing concerns about transmittable diseases, particularly HIV infection and hepatitis, which resulted in a dramatic increase in the use of NRL gloves. Escalating glove use in the 1990s was then associated

with the rise in reports of allergic reactions to NRL gloves among healthcare workers (23)(24)(25)(21)(26)(27).

The first case suggesting immediate-type hypersensitivity related to the use of latex was published in 1927 in German literature (26)(28), but the first clear description of immediate-type hypersensitivity was not published until 1979 (27).

The majority of risk groups for allergy development include health care workers, workers in the rubber industry, atopic individuals and children with congenital malformations (29)(30)(31)(32). Three types of pathological reactions can occur in people using latex medical gloves: irritant contact dermatitis, allergic contact dermatitis and immediate hypersensitivity. Hand dermatitis is shown to have a prevalence of 20% (16). Interestingly, occupational skin diseases as for example irritant and allergic contact dermatitis and contact uricaria are around one third of occupation-related complaints in the medical field. Allergens that must be taken into account for the evaluation of glove dermatitis are manifold: latex, rubber accelerators and other allergens related to rubber as well as the used dyes of the gloves (e.g. copper phthalocyanine) (for an exhaustive review please see (16). In addition, Natural rubber latex (NRL) was recognized as a major cause of IgE-mediated occupational asthma (OA) in the early nineties, especially in healthcare facilities (33). The latex allergy is caused by constituent components of latex gloves, rubber accelerators and added powders (34)(35)(36)(32)(37)(26)(21)(38)(39). Powder is used as a lubricant to ease donning of the gloves, but small amounts of powder are also used during manufacturing to facilitate stripping of the newly made glove. This explains why even powder-free gloves may contain minute amounts of powder. Latex proteins bind to powder particles in gloves and the powder can thus act as carrier of the allergen (25)(40)(41). The dust aerosol that can be created when donning and removing powdered gloves may increase the risk of allergic reactions because uptake, via the lungs, by people in the vicinity represents an additional route of exposure (23)(42).

The Scientific Committee on Medicinal Products and Medical Device, which has been asked to express its opinion on risks associated with the use of medical devices manufactured from NRL, concluded based on provocation studies that exposure to powder from latex-gloves can provoke allergic symptoms (asthma, rhinoconjunctivitis, urticarial, anaphylaxis) in latex-sensitized patients (41). This view is further reflected in the MEDDEV guideline 2.5/9 rev. 1 – Implications of the Medical Device Directives 93/42/EEC in relation to medical devices containing Natural rubber latex: A guide for manufacturer and notified bodies. In Germany, NRL as well as powder particles form NRL gloves were classified as airway- and skin sensitizing agents in the “Technical rules for hazardous substances (TRGS)” 907. In addition, the TRGS 540 states that powdered NRL gloves have to be substituted by powder-free and low-allergen latex gloves or other suitable gloves by employers. Subsequently, several studies investigated the effect of substitution of powdered gloves with non-powdered, protein-poor NRL gloves. The results support the assertion that substitution with non-powdered, protein-poor NRL gloves greatly reduces NRL sensitization and asthma (38). Moreover, powdered gloves have been implicated to increase adhesion and the formation of starch granuloma (43). Recently, a study with 340 female nurses in Thailand frequently using NRL gloves showed that sensitization to NRL was more prevalent in nurses that used NRL gloves with high proteins whereas as protein level range from 111-250 mg/dm^2 was determined in all tested gloves. Sensitization to NRL was shown to be associated with a decreased estimated forced expiratory flow that indicates narrow small airways of the lung. The authors conclude that the usage of gloves with low protein levels may reduce NRL allergen exposure that probably reduces the risk of NRL

sensitization and associated respiratory effects (4). A survey performed with HCWs estimated that latex exposure in HCWs contributes 3% of the total asthma related burden (14). In the United States, the FDA has currently determined that Powdered Surgeon's Gloves, Powdered Patient Examination Gloves, and Absorbable Powder for Lubricating a Surgeon's Glove present an unreasonable and substantial risk of illness or injury and that the risk cannot be corrected or eliminated by labeling or a change in labeling. Consequently, FDA is banning these devices (44). A reaction from Baid et al. (2) summarizes the findings on the usage of cornstarch powdered gloves, including promotion of wound infection, latex allergy, peritoneal adhesion and granulomatous peritonitis by cornstarch and expressed the need for a prohibition in India, too. Since also good powder free alternatives are available, the usage of powdered gloves seemed to be unnecessary (2). Srinivasan explains alternatives to powdered latex gloves to be non-powdered latex gloves and non-latex gloves. For people with latex allergy, nitrile or vinyl gloves are available. People without latex allergy may use non-powdered latex gloves, nitrile and/or vinyl gloves (1).

In addition, the negative aspect of NRL glove use, linked to the allergy problems, has gained substantial media coverage, in addition to the publication of a significant number of scientific papers. In reaction to the media and scientific coverage, and to rising compensation claims, many hospitals around the world have implemented new latex allergy and glove policies, resulting in the substitution of NRL gloves with synthetic gloves in certain areas, on specific patients or by sensitized staff. More recently, a number of high-profile hospitals, exemplified by Johns Hopkins Hospital in Baltimore, Md., USA, and the Cleveland Clinic's network of nine hospitals in Cleveland, Ohio, USA, have gone 'latex free'. As a result, a small but increasing number of medical practitioners only have access to gloves made from synthetic materials or latex gloves are only used in exceptional cases for tasks that require good tactile sensitivity. Such policies require full consideration of all of the factors involved, including also glove functionality as well as costs incurred, both directly and indirectly on the environment. Furthermore, also many changes were made in the production processes for NRL gloves (45). In Germany, Allmers et al. showed that healthcare facilities only purchase low-protein, powder-free NRL gloves, can even lead to prevention of sensitization (24). Additionally, in a case report it was shown that the switch from gloves containing diphenylguanidien as rubber accelerator to diphenylguanidine free gloves prevented recurrence of dermatitis (9). A further study showed that a contact allergy to rubber additives is significantly more often present in HCWs with hand eczema than in non-affected HCWs. A contact allergy to diphenylguanidine was found to be as common as allergy to thiurams (6). However, another study found that the presence of diphenylguanidin in gloves is more common than thiurams therefore the publication concluded the use of diphenylguanidine free gloves should be considered, to avoid contact allergies. Users that tested gloves without accelerators did not show any signs of allergies. Furthermore, the article rises the idea to add 1,3-diphenylguanidien to the European baseline series (8). Further data show, that the usage of accelerator free rubber gloves showed in a recent study with nine healthcare workers that switching from conventional gloves to accelerator-free gloves reduced or even healed the symptoms of hand eczema caused by wearing conventional gloves (5). In response to this, alternative rubber accelerators, such as dithiocarbamates and the so-called "accelerator-free" systems, are increasingly used in the manufacturing process.

In summary, those preventive measures against latex allergy as well as usage of synthetic rubber gloves, such as nitrile and vinyl has markedly reduced allergic reactions to latex-containing rubber gloves (37)(39)(38)(46).

2.3. Current knowledge and State of the art

Medical glove use by Health Care Workers (HCW) is recommended for two main reasons: 1) to reduce the risk of contaminating HCWs hands with blood and other body fluids: 2) to reduce the risk of germ dissemination to the environment and of transmission form HCWs to the patient and *vice versa*, as well as from one patient to another (21)(47).

In medical environments, natural rubber latex gloves are most common because of their excellent fit and handling characteristics, particularly related to their tactile sensitivity. Rubber latex is extracted from rubber trees, such as *Hevea braziliensis*. Natural rubber latex occurs in the latex vessels of the bark outside the phloem and the milky latex is collected by tapping the rubber tree bark (48)(49). NRL is a polymer of *cis*-1,4-isoprene. It is a milky, colloidal fluid comprised of 30-40% of rubber hydrocarbon particles suspended in a serum together with 55-65% of water, 5% of other non-rubber substances such as 1.1-2% of proteins, lipids, resins, and sugars, and some metals (48). In addition, during manufacturing various chemicals, such as accelerators, activators, anti-oxidants and vulcanizing agents are further added.

The level of proteins in NRL will vary to some extent and its bulk is in the aqueous phase. Some extractable proteins present in NRL have the potential to provoke an allergic reaction in some individuals. Over 200 different polypeptides have been identified in fresh NRL and 25% of them have been found to be responsible for allergic reactions caused by NRL (48)(26).

However, the processes used for NRL glove manufacture have changed greatly in recent years. One of the major changes was the switch from powdered gloves to chlorinated powder-free gloves: while removal of powder may have eliminated the possible transport of allergens, the concomitant lower allergenic potential may be coincidental. Chlorination usually involves a number of different processes, including acid neutralization and a number of leaching steps. It has been shown that the processes associated with chlorination (neutralization, washing with water) are almost equally as effective on their own without free chlorine, resulting in effective leaching of the proteins. The addition of a chlorination process during manufacture has been associated with lower levels of extractable proteins (EP). However, the leaching processes and finishing treatments necessary to remove residual chlorine and other chemicals appear to be responsible for the major reduction of allergenic protein levels (24).

The raw materials for synthetic glove manufacture include vinyl (polyvinyl chloride), nitrile (acetonitrile butadiene), neoprene, polyisoprene, polychloroprene, polyurethane and polyethylene, which are generally derived from oil chemistry (50). Nitrile is very similar in its polymer chemical structure to NRL and, in this respect, may be considered as synthetic latex (24). Thus, nitrile gloves are ideal for latex-sensitive patients. However, they are not as flexible as latex, which was also determined by the Scientific Committee on Medicinal Products and Medical Devices of the European Commission, and may cause type IV allergic reactions resulting in allergic contact dermatitis against the rubber additives (e.g. thiurams, dithiocarbamates, mercaptobenzothiazoles) that are necessary in their production (37). In addition, nitrile has a higher permanent set than latex, meaning that once stretched it does not fully recover (24). Thus, nitrile gloves tend to be designed

to fit more loosely than latex, and the combination of these properties may affect the users' tactile sensation and delicacy of touch. This has been confirmed by a study from Sawyer and Bennett in 2006, where participants noted that nitrile gloves that fitted their fingers were too narrow for their hands and gloves that fitted their hands were too large for their fingers. During this research, it was confirmed that there are detectable differences between nitrile and latex, where a pegboard test demonstrated an 8.6% increase in fine finger dexterity for latex over nitrile, although no differences related to gross dexterity. Whilst it is not clear at present what the practical effects of this research mean, it does appear that the stiffness of nitrile may affect user dexterity. The study also questioned users about their preferred material, with 67% preferring latex and 21% preferring nitrile (24). Interestingly, a study examined the effect of the fingernail length of dental students on the longevity of the protective barrier function and integrity of latex examination gloves. The result shows that the length of the fingernails significantly influences the integrity of the tested glove. Hence, the recommendation is to shorten fingernails below 1 mm by the clinician to reduce the risk of glove damage and the barrier function of the glove (3). In general, there is rising concern that anesthesia provider may transmit bacteria via gloves. Currently, one of the methods to avoid pathogen spread is to rub the gloves with an alcohol-based hand rub. It is not possible to change glove or wash hands. A study analyzed the influence on gloves integrity and safety by the usage of alcohol-based hand rub on common nitrile examination gloves. The results show that an alcohol based hand rub does not influence the safety and integrity of the tested gloves and did not hamper the performance of routine functions by the anesthesia provider (13). Interestingly, another study performed found that disinfection of hands with alcohol-based hand disinfectants before glove donning increased the amount of diphenylguanidine from polyisoprene gloves. Additionally, an experiment with artificial sweat was done to observe the amount of diphenylguanidine released over time from the respective glove. Results showed that even after a short exposure time, substantial amounts of dihenylguanidien are released (7). A modern approach to face the potential transmission of pathogens via glove usage is the modification of gloves equipped with an additional flap. This doffing aid that facilitates glove donning and thereof prevents contamination of users hands during glove removal. Results with 317 nurses and physicians showed that these modified gloves were able to reduce the hand and wrist contamination during glove removal compared to standard gloves (15).

Although vinyl gloves typically do not contain rubber additives and could theoretically serve as an alternative for type IV rubber accelerator allergic individuals, they have been found to be inferior in both durability and permeability and therefore less protective to microorganisms and chemotherapy drugs compared to other glove materials (latex, nitrile). Vinyl gloves contain phthalates, a plasticizer used in the manufacturing process of these gloves. Phthalates have been associated with impaired reproduction and human development as well as with breast cancer and lymphomas. A study on the permeability of 13 different gloves to 13 chemotherapy agents revealed vinyl gloves being the most permeable, even after short term application (37). A study performed in 2018 analyzed the different accelerators used in various nitrile, polychloroprene and NLR patient examination gloves. The most common accelerators were carbamates present in several glove type categories (in 90.5% of gloves). Other accelerators identified were thiurams, benzothiazoles, guanides and thioureas. Since the prevalence, this accelerant is very high, it is not astonishing that the sensitization to these kind of accelerant is quiet frequent. The study also revealed that manufacturers started to realize this harm and begun to produce rubber-accelerator-free gloves:

The analysis of those kind of gloves tested showed that the exact composition of the gloves still remained unknown without having data if these gloves are truly free of accelerators or if even new innovative accelerators or new crosslinking systems are being used. Furthermore the study also indicates that gloves produced with thermoplastic elastomers may be an alternative (17). However, currently they are not making widespread use in medical surroundings and they are not undisputed. A response to this publication mentions that manufacturers are not required to list the accelerators used in their product which may complicate the process of finding a safe alternative for the user and patient (18).

Tahir et al. analyzed the capability of *Streptococcus aureus*, a common cause of healthcare-associated infections, to be transferred within biofilms via glove usage. Therefore, the researchers contaminated nitrile, latex and surgical glove's fingertips with a culture of dry-surface biofilm and counted the numbers of colonies revealed after touching an agar plate with these gloved fingers. The results showed that all three types of gloves tested were able to transfer the bacteria. Interestingly, surgical gloves and nitrile gloves transferred more bacteria than latex gloves. Probably this is explained by the latex glove being the most hydrophobic glove type (12). A new trend is to develop antimicrobial-impregnated gloves that may reduce contamination of the surrounding, hence reducing the development of healthcare-associated infections. In a study, poly-hexamethylene biguanide hydrochloride (PHMB) -treated gloves showed a lower amount of transferred common hospital pathogens (*Streptococcus pyogenes*, carbapenem-resistant *E.coli*, MRSA and ESBL-producing *Klebsiella pneumoniae*) than non-treated gloves. Nevertheless, a good hand hygiene practice and glove changing in addition has to be considered in addition (10).

In summary, it can de determined that a variety of factors, including glove strength, abrasive resistivity, dexterity and comfort, should be taken into account when selecting gloves for specific needs (24). However, with the reduced incidence of allergic reaction, the availability of specific and sensitive testing for the selection of low-allergenic gloves, competitive costs and lower environmental impact, natural rubber latex (NRL) remains an excellent choice of material for medical gloves (24). Nevertheless, it can also be concluded that the use of powder on latex gloves present numerous risks to patients and healthcare workers as described previously. In addition, since there are many non-powdered gloves available that have the same level of protection, dexterity, and performance – powdered gloves cannot be regarded as state of the art. Moreover, the non-powdered alternatives do not carry any of the risks associated with glove powder and hence the risks for patients and health care workers posed by powdered gloves seem to be unreasonable and substantial.

3. Device under evaluation

3.1. Type of evaluation

Sri Trang Gloves (Thailand) Public Company Limited, as a medical device manufacturer, is obligated to conduct a clinical evaluation in accordance with the requirements set out in Annex XIV of the MDR 2017/745 within the framework of CE-marking in order to provide sufficient proof that the products under evaluation conform to the state-of-the-art technology when in clinical use.

The MDR 2017/745 further defines the requirements for the clinical evaluation. The manufacturer is obligated to provide evidence based clinical data that the device meets the general safety and performance requirements (Annex I) concerning safety and performance under normal condition of use. Furthermore, the manufacturer is intended to evaluate the side effects and the acceptability of the risk/benefit ratio on the available clinical data.

However, article 61 10. of the MDR states *„Without prejudice to paragraph 4, where the demonstration of conformity with general safety and performance requirements based on clinical data is not deemed appropriate, adequate justification for any such exception shall be given based on the results of the manufacturer's risk management and on consideration of the specifics of the interaction between the device and the human body, the clinical performance intended and the claims of the manufacturer. In such a case, the manufacturer shall duly substantiate in the technical documentation referred to in Annex II why it considers a demonstration of conformity with general safety and performance requirements that is based on the results of non-clinical testing methods alone, including performance evaluation, bench testing and pre- clinical evaluation, to be adequate.“*

The current guideline on medical devices “clinical evaluation: a guide for manufacturers and notified bodies” (MEDDEV 2.7.1, revision 4) further specifies in section 10.3 how to demonstrate conformity with the general performance and safety related requirements without clinical data.

In line with article 61 10.cand section 10.3 of the current MEDDEV 2.7.1 guideline, demonstration of conformity with safety and performance related essential requirements based on clinical data is not deemed appropriate for the non-sterile examination gloves (latex powdered, latex powder free and nitrile - powder free). The rationale is based on the intended use of the device, the device/body interaction and considerations of the risk management. A detailed justification is given in the following section (3.2 Justification for exclusion of need of clinical data).

The clinical evaluation was structured as suggested in Annex A9 of the current MEDDEV 2.7.1 guideline, including the new requirements that are mentioned in the MDR.

3.2. Justification for Exclusion of Need of Clinical Data

The non-sterile examination gloves (latex powdered, latex powder free and nitrile - powder free) are single-use devices intended for medical purposes that is worn on the examiners hand or finger to prevent contamination between patient and examiner.

The clinical evaluation for the examination gloves is based on recognized harmonized product specific standards or common specifications without clinical data. Due to the device type, which is clearly defined in the product standard and the widespread use of the device as well as the long clinical history, evidence does not need to be based on a systematic literature search or clinical trial.

In addition, the risk management process for the non-sterile examination gloves (latex powdered, latex powder free and nitrile - powder free), the post-market surveillance data as well as the search in database of the German competent authority BfArM and the American FDA did not reveal any additional risks that has not been considered yet and for which clinical data would have been necessary. The clinical performance of the device is demonstrated by the manufacturer. Furthermore, claims made by the manufacturer and described in part 2.5 of this document are addressed adequately in the respective documents provided by the manufacturer and do not need any further data exploration.

Taken together, the efficiency and safety of the non-sterile powdered latex, powder-free latex and nitrile examination gloves do not need to be demonstrated by clinical data as these products are already used for nearly 30 years and are therefore well established in literature as demonstrated in section 3 of this clinical evaluation. Furthermore, performance and safety related aspects for the sterile examination gloves are defined in product specific harmonized standards.

In the following sections 4.3 and 4.4, the data provided by the manufacturer and the compliance to specific general safety and performance requirements is demonstrated in detail.

3.3. Demonstration of equivalence

This section is not applicable since this clinical evaluation is not based on clinical data from literature or their equivalent products.

3.4. Data provided by the manufacturer

3.4.1. Applied standards and regulations

A list with the applied standard and regulations was extracted from the technical file of the products and displayed below:

MDR (EU) 2017/745	Medical Device Regulation
PPE (EU) 2016/425	Personal Protective Equipment Regulation
ISO 13485: 2016	Medical devices - Quality management systems - Requirements for regulatory purposes
ISO 9001: 2015	Quality management systems – requirements
ISO 14971: 2019	Medical devices - application of risk management to medical devices
EN 455-1: 2000	Requirements and testing for freedom from holes
EN 455-2: 2015	Requirements and testing for physical properties
EN 455-3: 2015	Requirements and testing for biological evaluation
EN 455-4 : 2009	Requirements and testing for shelf life determination
ISO 10993-1: 2018	Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process
ISO 10993-5: 2009	Biological evaluation of medical devices – Part 5: Test for in vitro cytotoxicity
ISO 10993-10: 2010	Biological evaluation of medical devices – Part 10: Test for irritation and skin sensitization
ASTM F1671: 2013	Standard test method for resistance of materials used in protective clothing to penetration by blood-borne pathogens using phi-x174 bacteriophage penetration as a test system
ASTM D3578: 2019	Standard specification for rubber examination gloves
EN 1041: 2008+A1: 2013	Information supplied by the manufacturer of medical devices
EN ISO 15223-1: 2016	EN ISO 15223-1 Symbols to be used with medical device labels, labelling and information to be supplied
ASTM D7160: 2016	Determination of expiration dating for medical gloves
ASTM D7161: 2016	Determination of real time expiration dating of mature medical gloves stored under typical warehouse conditions
EN 420: 2003+A1: 2009	Protective gloves - General requirements and test methods
EN ISO 374-1: 2016+A1: 2018	Protective gloves against dangerous chemicals and micro-organisms - Part 1: Terminology and performance requirements for chemical risks
EN 374-2: 2014	Protective gloves against dangerous chemicals and micro-organisms - Part 2: Determination of resistance to penetration
EN 374-4: 2020	Protective gloves against chemicals and micro-organisms - Part 4: Determination of resistance to degradation by chemicals
EN ISO 374-5: 2016	Protective gloves against dangerous chemicals and microorganisms - Part 5: Terminology and performance requirements for microorganisms risks
EN 16523-1: 2015+A1: 2018	Determination of material resistance to permeation by chemicals - Part 1: Permeation by liquid chemical under conditions of continuous contact

3.4.2. Risk management

Sri Trang Gloves (Thailand) Public Company Limited has provided a risk management plan, a risk management report and a risk management file for the latex powdered (non-sterile), latex powder free (non-sterile) and nitrile powder free (non-sterile) examination gloves in order to identify hazards associated with the products, to estimate and evaluate the associated risks, to control these risks and to monitor the effectiveness of the controls. The drawn conclusion by the manufacturer are described in the technical file part 5 „benefit-risk analysis and risk management“ of each product.

The provided risk analysis is in compliance with Annex I of the MDR 2017/745 and covers the whole entire lifecycle of the device in question.

Based on the conducted risk analysis of the **latex powder free (non-sterile) and nitrile powder free (non-sterile)** examination gloves foreseeable risks have been identified by the manufacturer and evaluated in most cases as acceptable with respect to the intended application and use of the products. Counteractions have been taken for those items for which an initially unacceptable risk has been identified. Subsequently, the performed implementations were verified. Finally, it can be assumed that no unacceptable residual risk exists with the products either individually or cumulatively, that outweighs the benefits from the use of the products.

This also applies to the **latex powdered gloves (non-sterile)**. Furthermore, the risk due to powder was also assessed, and a reduction in the amount of powder is sought, but the increased allergy-causing potential due to powder-transported latex proteins was not taken into account by an action that effectively minimize the risk. According to literature, which was analyzed for the establishment of the “medical background, current knowledge and state-of-the art”, it was already shown in the 1990s that modified cornstarch could act as a vector for allergic latex proteins and precipitate a life-threatening allergic reaction in sensitized patients (22)(24). In addition, currently the FDA has determined that powdered gloves present an unreasonable and substantial risk of illness and injury and that the risk cannot be corrected or eliminated by labeling or a change in labeling. Consequently, FDA is banning these devices (44). In addition also in Germany, the substitution of powdered gloves by unpowdered gloves has become mandatory, since inhaling of latex protein bound to cornstarch has been categorized as sensitizer of the respiratory tract (22).

Finally, it is to be noted that some risks are not mentioned in the provided risk analysis but they are considered in the label or the technical file like

- For individual use only
- It is necessary to change the gloves in case of any defect, puncture, damage, contamination, etc.
- Keep in dry condition and avoid the sunlight or other ozone sources
- Keep away from insects

Therefore, the approaches to minimize the risks and the verifications of those approaches are not described. It is recommended to extend the risk analysis by those aspects.

3.4.3. Risk-benefit ratio

Since the benefit for the user and patient of the latex powder free (non-sterile) and nitrile powder free (non-sterile) examination gloves is evaluated as high and the performed risk analysis shows

that all risks considered are evaluated as acceptable the identified benefits clearly overweigh the remaining risks.

However, regarding the latex powdered gloves (non-sterile) the evaluation of overall residual risk acceptability and the risk-benefit analysis did not explicitly take into account the potential risk of powder-transported latex proteins.

3.4.4. PMS data

In the course of the last clinical evaluation in 2017, the results of the postmarked surveillance data led to the conclusion that the latex and nitrile examination gloves are safe for the user and the patient. Additionally, the last overall meeting on PMS was performed beginning of 2020. The minutes were provided by the manufacturer and it is concluded, that the products are still under safety, quality and performance of medical devices as required (see document SCT.QA.FO.19.002-010419 R.00_Feedback Report Year 2019; dated 2020-01-16). According to the manufacturer, a new style of PMS report is in preparation. Hence, the data acquisition for a proactive PMS and customer surveillance will start in Q3 of 2020. The manufacturer agrees to include these data in the next update of the clinical evaluation. Within the update of this clinical evaluation, the latest data for 2019 were further evaluated (from document „Summary_Customer_Satisfaction_Year 2019“ and „Adverse event reporting. competitor analysis. interview with customers“).Importantly, there were no critical complaints in regards to alleged deficiencies that would have required a recall or withdrawal of the product from the market. Additionally, the company states that there was no competent authority post-market surveillance inquiry or an adverse event reporting required.

The competitor analysis states that the gloves are able to compete with the products on the market from other manufacturers.

Customer complaints are documented and extensively analyzed in the document „Complaint Raw data 2019 all products sterile non-sterile“.

It can be stated that the determined complaint rates reside in a general accepted level.

Specifically, the very low complaint rates for holes are in favor for the safety of the devices.

The manufacturer additionally performs literature search and review of the publications (Literature Searches and Review 2019) as well as updates the applied standards and regulations (Standard regulation updated_Report 2019; Standard regulation updated_Support 2019) on a frequent basis to ensure up to still produce a safe product that complies with the newest regulations.

In regards to the performed search for safety related notices in the database from the German competent authority, two recall notices were found. It has to be clearly stated, that those recalls were from 2006 and 2013 and from other manufacturers than Sri Trang Gloves (Thailand) Public Company Limited. However, the cause of the recalls can be transferred to evaluate the safety and performance of any examination glove and therefore the notices should not be ignored. The first recall from 2006 deals with Micro-Touch Ultra PF latex examination gloves from Ansell Healthcare Europe. Here, the indicated shelf life of the gloves may not be as stated on the labelling. The risk of wrong labeling may occur on any product and should be evaluated in the course of the risk management. The last recall was performed by HPC Healthline UK Limited for GN85 violet accelerator free nitrile gloves due to a manufacturing anomaly that may cause an increased fire risk when transported and then exposed to air. Since this recall is related to the manufacturing process

of the gloves, also risks that might occur during the manufacturing process should be considered. The FDA MAUDE database for adverse event reports revealed three reports. On led to a recall of powder-free nitrile patient examination gloves by the manufacturer SVS LLC since they contain a not further described fine glitter on the glove's surface (report number 8590804). The second report was on ripped CURAD vinyl patient examination gloves (report number 6600794). The risk with ripped gloves is addressed by Sri Trang Gloves (Thailand) Public Company Limited. The last identified report was from Vital shield gold gloves concerning the non-sterile medical examination gloves size 9 powdered (report number MW5017548). Here, a patient had an adverse reaction to a dental procedure. Unfortunately, no further information is given, making it difficult to draw conclusion out of this report.

Overall, the overall low complaint rate, the absence of safety notes in the database of the German competent authority for the devices under question and the very low amount of relevant notices to other examination gloves found in the two databases without time restriction must be seen as evidence for the safety of the devices covered by this clinical evaluation.

3.4.5. Pre-clinical and non-clinical tests

The non-sterile examination gloves (latex powdered, latex powder free and nitrile - powder free) do not possess any special design features that pose special safety concerns identified during the risk analysis for the gloves (refer to section 4.3.1) and that required further evaluation from a clinical perspective. Moreover, safety and performance related aspects of the non-sterile examination gloves are fully covered by harmonized and other relevant standards as well as performance evaluation, bench testing and pre-clinical evaluation. To provide an overview of those pre-clinical and non-clinical tests, the relevant data is summarized in the table below and analyzed in section 3.5 of this document.

The manufacturer explains that biocompatibility testing are performed for nitrile and latex gloves. The latex gloves are only produced and tested in natural color. However, the nitrile gloves are available in different colors, hence the manufacturer provided biocompatibility testing for the different colors and explains that the colors „violet blue" and „blue" are tested frequently since these are the most sold colors. Since some tests do not indicate the color of the tested glove, the manufacturer is able to trace the indicated barcode of the tests to allocate the right color of the glove tested. Random testing with different colors available were also performed by the manufacturer. All test confirm the biocompatibility of tested colored gloves. An overview of the tests performed can be seen in the following tables. A detailed list of tests to the different glove colors are shown in the tables below as well. To furthermore confirm the safety of the different colored gloves, MSDS sheets are collected by the manufacturer for the color pigments blue (SCT.LA.SP.10.012_Blue Pigment), violet blue/ dark blue (SCT.LA.SP.10.116_Violet Blue. Dark Blue Pigment), pink (SCT.LA.SP.10.128_Pink Pigment), ocean blue/ dark ocean blue (SCT.LA.SP.10.149_Ocean Blue. Dark Ocean Blue Pigment) and black (SCT.LA.SP.10.159_Black Pigment).

Table 4: Tabulation of the data used in the evaluation with categorization according whether they address performance, safety or both. The referenced test is also indicated. A short tendency of the test result is given.

Verified characteristics	Standard for reference	Test report	Involved device	Relevant for	Type of study	Tendency of the evidence (favorable/ unfavorable/indifferent)
Cytotoxicity	EN ISO 10993-5	1151969-S01 1156407-S01.1 1151967_S01 1151974-S01 1023198-S01 1151990-S01 1156408-S01.1 1068431-S01 1229894-S01	LC01 LO01 LX01 NC01 NC02 NO01 NO02 NO03 NO04	Safety	In-vitro test	favorable
Irritation	EN ISO 10993-10	1032449-S01 19-02021-G2 7191201528-01-00_CR1 1152034-S01 1012172-S01.1 7191203168-01-00 7191201527-01-00_CR1 2191084741-01-00 1229896-S01	LC01 LO01 LX01 NC01 NC02 NO01 NO02 NO03 NO04	Safety	In vivo animal test	favorable
Skin sensitization	EN ISO 10993-10	1031748-S01 19-02021-G1 7191201528-02-00_CR1 1152033-S01 1019495-S01 7191203168-02-00 7191201527-02-00_CR1 2191084741-02-00 1229895-S01	LC01 LO01 LX01 NC01 NC02 NO01 NO02 NO03 NO04	Safety	In vivo animal test	favorable
Viral penetration	ASTM F 1671	1152456-S01 1156409-S01.1 1149901-S01 1152458-S01 1023199-S01 11523455-S01 1156410-S01.1 1068432-S01 1229893-S01	LC01 LO01 LX01 NC01 NC02 NO01 NO02 NO03 NO04	Safety	In vitro test	favorable

Verified characteristics	Standard for reference	Test report	Involved device	Relevant for	Type of study	Tendency of the evidence (favorable/ unfavorable/indifferent)
Freedom from holes	EN 455-1	7191205854-EEC19/01-WBH 7191205017-EEC19/02-WBH 7191205017-EEC19/01-WBH 7191205017-EEC19/03-WBH 7191180515-EEC18/04-CSL 7191205017-EEC19/05-WBH 7191205855-EEC19/01-WBH 7191189336-EEC18/01-WBH 7191221625-EEC19/03a-WBH	LC01 LO01 LX01 NC01 NC02 NO01 NO02 NO03 NO04	Performance	Mechanical test	Favorable
Dimension	EN 455-2	7191205854-EEC19/02-WBH 7191205139-EEC19/02-WBH 7191205139-EEC19/01-WBH 7191205139-EEC19/03-WBH 7191180515-EEC18/01-CSL 7191205139-EEC19/05-WBH 7191205855-EEC19/02-WBH 7191189336-EEC18/02-WBH 7191221625-EEC19/03b-WBH	LC01 LO01 LX01 NC01 NC02 NO01 NO02 NO03 NO04	Performance	Mechanical test	favorable
Tensile	EN 455-2	7191205854-EEC19/03-WBH 7191205139-EEC19/07-WBH_CR1 7191205139-EEC19/06-WBH_CR1 7191205139-EEC19/08-WBH_CR1 7191180515-EEC18/02-CSL 7191205139-EEC19/10-WBH_CR1 7191205855-EEC19/03-WBH 7191189336-EEC18/03-WBH 7191221625-EEC19/03c-WBH	LC01 LO01 LX01 NC01 NC02 NO01 NO02 NO03 NO04	Performance	Mechanical test	favorable
Residual powder	EN 455-3	7191205854-CHM19-JS-05 7191205723-CHM19-JS-02-CR1 7191205723-CHM19-JS-01-CR1 7191205723-CHM19-JS-03-CR1 7191180515-CHM18/03-JS 7191205723-CHM19-JS-04-CR1 7191202751-CHM19/02-JS 7191189717-CHM18/01-JS 7191221625-CHM19-02-JS	LC01 LO01 LX01 NC01 NC02 NO01 NO02 NO03 NO04	Safety	Analytical test	favorable
Protein	EN 455-3	LGM/BTK/UPB/5.10/CP/1804/0070 LGM/BTK/UPB/5.10/CP/1804/0169 7191205724-CHM19-JS-01-CR1	LC01 LO01 LX01	Safety	Analytical test	19 µg/g (LC01) 23 µg/g (LO01) 131.3 µg/g (LX01)

Verified characteristics	Standard for reference	Test report	Involved device	Relevant for	Type of study	Tendency of the evidence (favorable/ unfavorable/indifferent)
Stability and shelf life	EN 455-4	STGTSR-SL-19-004	LC01	Safety and Performance	Mechanical and analytical test	Shelf life up to 5 years
		STGT-HY-SL-13-003	LO01			Shelf life up to 5 years
		STGT-HY-SL-14-003	LX01			Shelf life up to 5 years
		STGT-HY-SL-10-001	NC01			Shelf life up to 5 years
		STGT-HY-SL-18-001	NC02			Shelf life up to 3 years
		STGT-HY-SL-11-002	NO01			Shelf life up to 5 years
		STGTSR-SL-19-001	NO02			Shelf life up to 5 years
		STGT-HY-SL-18-002	NO03			Shelf life up to 3 years
		STGTSR-SL-20-002	NO04			Shelf life up to 3 years

*Table 5: References and summary of performed **cytotoxicity assays** separated by the different glove types and available colors.*

Product code	Material	Available colors	Study number	Test result (undiluted/different dilutions)
NC01	nitrile	white	No data available	
		pink	1031751-S01	Pass (1:2, 1:4, 1:8 and 1:16 dilution)
		blue	1152011-S01	Pass (1:2, 1:4, 1:8 and 1:16 dilution)
		violet blue	1151974-S01	Pass (1:2, 1:4, 1:8 and 1:16 dilution)
		black	1031752-S01	Pass (1:2, 1:4, 1:8 and 1:16 dilution)
		ocean blue	No data available	
NC02	nitrile	violet blue	1023198-S01	Pass (1:2, 1:4, 1:8 and 1:16 dilution)
NO01	nitrile	blue	151990-S01	Pass (1:2, 1:4, 1:8 and 1:16 dilution)
NO02	nitrile	violet blue	1156408-S01.1 Amended	Pass (1:8 and 1:16 dilution)
		black	1080897-S01	Pass (1:8 and 1:16 dilution)
		dark ocean blue	No data available	
		ocean blue	1130416-S01	Pass (1:8 and 1:16 dilution)
		white	No data available	
		dark blue	961196-S01	Pass (1:8 and 1:16 dilution)
NO03	nitrile	black	1231183-S01	Pass (undiluted, 1:2, 1:4, 1:8 and 1:16 dilution)
		white	1231182-S01	Pass (undiluted, 1:2, 1:4, 1:8 and 1:16 dilution)

Product code	Material	Available colors	Study number	Test result (undiluted/different dilutions)
		violet blue	1068431-S01	Pass (undiluted, 1:2, 1:4, 1:8 and 1:16 dilution)
NO04	nitrile	violet blue	1229894-S01	Pass (1:8 and 1:16 dilution)
		white	No data available	
		ocean blue	No data available	

*Table 6: References and summary of performed **irritation testing** separated by the different glove.*

Product code	Material	Available colors	Study (report) number	Test result
NC01	nitrile	white	BIO-ATX 436	Non-irritant
		pink	1032450-801	Negligible irritant
		blue	1152038-S01	Negligible irritant
		violet blue	1152034-S01	Negligible irritant
		black	1032451-S01	Negligible irritant
		ocean blue	No data available	
NC02	nitrile	violet blue	1012172-S01.1 Amended	Negligible irritant
NO01	nitrile	blue	7191203168-01-00	Negligible skin irritation response
NO02	nitrile	violet blue	7191201527-01-00_CR1	Negligible skin irritation response
		black	7191203167-01-00	Negligible skin irritation response
		dark ocean blue	No data available	
		ocean blue	7191203167-01-00	Negligible skin irritation response
		white	No data available	
		dark blue	No data available	
NO03	nitrile	black	1231188-801	Negligible irritant
		white	1231186-S01	Negligible irritant
		violet blue	2191084741-01-00	Negligible irritant
NO04	nitrile	violet blue	1229896-S01	Negligible irritant
		white	No data available	
		ocean blue	No data available	

Table 7: References and summary of performed ***skin sensitization tests*** *separated by the different glove.*

Product code	Material	Available colors	Study (report) number	Test result
NC01	nitrile	white	BIO-ATX 435	No sensitizing effect seen
		pink	1031747-S01	No sensitizing effect seen
		blue	1152037-S01	No sensitization response
		violet blue	1152033-S01	No sensitization response
		black	1030692-S01	No sensitizing effect seen
		ocean blue	No data available	
NC02	nitrile	violet blue	1019405-S01	No sensitizing effect seen
NO01	nitrile	blue	7191203168-02-00	No skin sensitization
NO02	nitrile	violet blue	7191201527-02-00_CR1	No skin sensitization
		black	7191203168-02-00	No skin sensitization
		dark ocean blue	No data available	
		ocean blue	No data available	
		white	No data available	
		dark blue	No data available	
NO03	nitrile	black	1231187-S01	No skin sensitization
		white	1231185-801	No skin sensitization
		violet blue	2191084741-02-00	No skin sensitization
NO04	nitrile	violet blue	1229895-S01	No skin sensitization
		white	No data available	
		ocean blue	No data available	

Table 8: References and summary of performed ***viral penetration*** *tests separated by the different glove.*

Product code	Material	Available colors	Study number	Test result
NC01	nitrile	white	780248	Pass
		pink	1031753-S01	Pass
		blue	1152457-S01	Pass
		violet blue	1152458-S01	Pass
		black	1031754-S01	Pass
		ocean blue	No data available	
NC02	nitrile	violet blue	1023199-S01	Pass
NO01	nitrile	blue	1152455-S01	Pass
NO02	nitrile	violet blue	1156410-S01.1 Amended	Pass
		black	1083395-S01	Pass
		dark ocean blue	No data available	
		ocean blue	1127210-S01	Pass
		white	No data available	
		dark blue	No data available	
NO03	nitrile	black	1231178-S01	Pass
		white	1231177-S01	Pass
		violet blue	1068432-S01	Pass
NO04	nitrile	violet blue	1229893-S01	Pass
		white	No data available	
		ocean blue	No data available	

3.5. Analysis of the collected data

3.5.1. Requirements on performance (Section 1 of Annex I) and safety (Section 1 and 8 of Annex I)

Medical gloves are legally covered by the MDR 2017/745 and the European Standard 455.

According to the product specific standard 455-1 (Medical gloves for single use - Part 1: Requirements and testing for freedom from holes) medical gloves for single use, which are used in the medical environment to protect the user and the patient from contamination, have to be free of holes. This requirement is supposed to be fulfilled in case that the test method outlined in section 5 of the standard does not detect any leakage of the device.

The respective color and size of the tested latex powdered (non-sterile) examination gloves, Latex powder free (non-sterile) examination gloves and nitrile powder free (non-sterile) examination gloves fulfill the requirement of freedom from holes according to the test method outlined in the standard 455-1.

The requirements for the physical properties of examination gloves are defined in the second part of the harmonized standard 455-2:2009. According to the standard, the test sample has to be inspected with regard to length, width, force at break and force at break after challenging.

The scope of the EN 455-3 is to specify requirements for biological safety of medical gloves, by stipulating labeling and test methods. The requirements in EN 455-3 concerning labeling of medical gloves are summarized in table 2.

Table 9: Table 2. Labeling requirements for medical gloves for single use in EN 455-3.

- Gloves containing natural rubber latex shall be labeled on the packaging with a latex symbol, with an attached allergy warning text
- Glove labeling supposing low amounts of latex allergens shall be avoided
- The labeling shall indicate if the gloves are powder-free or powdered
- If the protein content is labeled, the process limit shall be represented
- Glove labeling shall not include any term suggesting relative safety

In the normative annex, the test method for extractable proteins is presented – a modified Lowry assay. At first, the amount of extractable protein has to be analyzed. The determination of extractable protein is only mandatory for gloves based on natural rubber. Therefore, the nitrile powder free (non-sterile) examination gloves do not have to be tested with this method. The stipulated values of 50 µg/g for non-powdered and 150 µg/g for powdered examination gloves should not be exceeded.

Further questions dealt with in EN 455-3 are the presence of endotoxins, glove chemicals, and powder. For gloves to be labeled as „powder-free“, according to this standard the total amount of powder residue for powder free gloves is not allowed to be more than 2mg for each glove otherwise the glove has to be defined as a powdered glove. Depending on their method of manufacture, some medical gloves can have on their surface a small amount of powder, normally modified cornstarch, which is intended to assist donning. Current thinking is that the presence of excessive amounts of such powder can present a health hazard. The removable surface powder of the gloves was determined according to ASTM D6124:2006 (reapproved 2011). The ASTM D 6142 method is equivalent to the method outlined in EN ISO 21171:2006. The results show that only the powdered

latex examination glove exceeded the 2 mg/glove value, all other tested products revealed values far below 2 mg/glove.

Finally, the requirements of the EN 455-3 regarding the labeling of the examination gloves were analyzed (see table 4).

Table 10: Assessment of the fulfillment of the labeling requirements for medical gloves for single use.

	Latex gloves powdered	Latex gloves powder-free	Nitrile powder-free gloves
Gloves containing natural rubber latex shall be labeled on the packaging with a latex symbol, with an attached allergy warning text	✓	✓	Not applicable
Glove labeling supposing low amounts of latex allergens shall be avoided	Not applicable	Not applicable	Not applicable
The labeling shall indicate if the gloves are powder-free or powdered	✓	✓	✓
If the protein content is labeled, the process limit shall be represented	Not applicable	Not applicable	Not applicable
Love labeling shall not include any term suggesting relative safety	Not applicable	Not applicable	Not applicable

Within the framework of the labeling review, based on the provided documents, the non-sterile examination gloves (latex powdered, latex powder free and nitrile - powder free) fulfill the labeling requirements of EN 455-3.

The fourth part of the product specific standard 455-4:2009 asks for the determination of the appropriate shelf life of the gloves. Glove samples were randomly selected directly after production and tested according to EN 455-1, EN 455-2 and EN 455-3. Afterwards, accelerated aging and real-time aging was performed according to the test method outlined in 455-4. Based on the accelerated aging results a shelf life of up to 3 or 5 years was determined for the respective gloves (see table 4). The packaging displays the manufacturing date, expiration date and lot number according to EN 980:2008 and EN 1041:2008 (see technical documentation).

In addition, the EN-455-3 states in section 4.1 that medical gloves for single use have to be evaluated according to EN ISO 10993. Based on EN ISO 10993-1 medical gloves are categorized as device with limited contact duration and require compliance with EN ISO 10993-5 and EN ISO 10993-10. Therefore, biocompatibility of the latex powdered and powder-free (non-sterile) and the nitrile powder free (non-sterile) examination gloves was verified by *in vitro* tests as well by a bioassay in rabbits and guinea pigs. Cytotoxicity according to EN ISO 10993-5 was evaluated with the help of the Minimal Essential Media (MEM) Elution test for extractable substances. Test samples and controls were extracted in 1xMinimal Essential Media with 5% bovine serum for 24-25 hours at 37°C±1°C with agitation. Different dilutions of the test article extract (undiluted, 1:2, 1:4, 1:8 and 1:16) and appropriate controls were added to monolayers of standard L-929 cells (ATCC CCL-1) in triplicates and incubated until approximately 80% confluence was reached. Afterwards the monolayers were examined and scored based on the degree of cellular destruction. Based on the results, it can be assumed that the non-sterile examination gloves do not exert a cytotoxic effect on L-929 cells.

The assessment of the examination glove regarding its potential to induce skin irritation or sensitization was done for the devices under evaluation in an applied in-vivo test model. The

evaluation was performed with 3 New Zealand White rabbits using a single dermal application of 25mm x 25mm of the test article on two test sites, both non-abraded. Appropriate controls were included. The test sites were semi-occluded for 4 hours and observed individually for erythema, edema and other effects 1, 24, 48 and 72 hours after unwrapping and the primary irritation index was determined. The tested products elicited a negligible dermal response in the rabbits under the conditions of this test.

The sensitization potential of the different examination gloves was tested in guinea pigs (Hartley-strain). Additional animals served as controls (positive and negative). Each animal in the test group received a topical application of the test article up to three times per week during consecutive weeks. Two weeks after the last topical induction, the challenge application was made at virgin sites for 6 hours. Erythema, edema and other effects were recorded 24 and 48 hours after the challenge application. Here, the test articles did not elicit a sensitization reaction in the animals under the conditions of the test.

Finally, the manufacturer conducted viral penetration tests according to ASTM F1671. The test evaluates the barrier function of protective materials that are intended to protect against blood borne pathogen hazards. After conditioning of the gloves tested, the product was tested for viral penetration by using ΦX174 bacteriophages. After incubation time and washing steps, the final amount of bacteriophages left were determined. Adequate controls were included consisting of a negative and a positive control. All products tested passed the test with no visual penetration seen.

With respect to the different color of the gloves, the manufacturer performed cytotoxicity, irritation and sensitization as well as viral penetration test with the different available colored glove types. The results showed that all tested colored gloves passed to biocompatibility testing whereas applied positive or negative controls, where applicable, were as expected.

As described in the references tests and summarized in the text above, all tested products passed the cytotoxicity, irritation and sensitization test, whereas applied controls were within acceptable parameters. The final evaluation of the test results is done by Sri Trang Gloves (Thailand) Public Company Limited and can be found in section 6.1 (pre-clinical and clinical data → biocompatibility) of the technical documentation.

In summary, the non-sterile examination gloves (latex powdered, latex powder free and nitrile - powder free) fulfill the requirements of the performed product tests according to EN 455-1, 455-2, 455-3 as well as EN ISO 10993-5 and 10993-10 and EN 455-4.

Since the European standard EN 455 defines the safety and performance specific requirements for medical gloves for single use, compliance of the non-sterile examination gloves (latex powdered, latex powder free and nitrile - powder free) with the requirements of EN 455 demonstrates that the examination gloves are in conformity with the relevant general safety and performance requirements (GSPR) of the MDR 2017/745 (Annex I).

3.5.2. Requirements on risk/benefit ratio (Section 2 of Annex I)

The manufacturer identified risks associated with the product and conducted a risk analysis for each product. Identified risks are adequately addressed, mainly by including the respective symbol as warning and precaution on the glove box to inform the user. The remaining risks are evaluated as acceptable by the manufacturer and it is determined that no unacceptable residual risk exists either individually or cumulatively that would outweigh the benefits associated with the usage of

the product. The benefit to the user clearly overweighs the remaining risks for the non-powdered examination gloves when the product is used as intended and the precautions and warnings given by the manufacturer are considered. Prevention of contamination in the health care environment is one of the most crucial hygienic action to avoid spread of pathogenic agents. However, it was found during the clinical evaluation, that the risk of powder as vector for allergens in the powdered latex examination gloves may not be state of the art anymore. Additionally, the powder might also be involved in other illnesses than allergy like inflammation. Here, it is debatable if the risk for the user really overweighs the benefit since many adequate alternatives are available on the market.

3.5.3. Conformity with the requirements on acceptance of undesirable side-effects (Section 8 of Annex I)

The here described examination gloves are medical devices that prevent contamination between patient and examiner. If used as intended with attention to the warnings and precautions mentioned on the box, the gloves can be applied without concerns for side effects, as it is not affecting any physical function of the user. For the NRL gloves, the undesirable side effects may be mainly the rising risk of allergy induction, which is not a risk that arises from the examination glove itself, but is more a risk caused by the latex material. Using latex gloves means accepting this risk. The manufacturer minimizes these risks by the respective warning symbol on the glove box. For the powder containing gloves, it has to be clearly stated, that as shown in various publications, the powder may induce allergies more strongly and this seems to be an undesirable side effect that could be prevented by the use of adequate alternative products that are available. However, the manufacturer also indicates the powder containing gloves as such, so that it is obvious to the user. The analysis and conclusion of the risk management, the tests performed according to ISO 10993-1, the long market experience with the here covered examination gloves as well as the absence of relevant safety notes in the BfArM and MAUDE database for these devices further show that no undesirable side-effects than the presence of powder (as identified in the literature search) need to be reevaluated for the devices.

4. Conclusion

For the non-sterile **non-powdered** examination gloves the following can be stated:

The clinical evaluation clearly demonstrates that the non-sterile examination gloves (latex powder free and nitrile - powder free) are in conformity with the relevant general safety and performance requirements of MDR 2017/745 (Annex I) by compliance to the requirements of EN 455. The current information material is considered adequate with respect to the intended user.

The performance and safety of latex powder free (non-sterile) and nitrile powder free (non-sterile) examination gloves have been established and risk associated with the use of these devices are acceptable when weighed against the benefits to the patient.

Taken together, the performance and safety of the devices have been established and risks associated with the use of the devices are acceptable when weighed against the benefit for the user and patient.

For the non-sterile **powdered** examination gloves the following can be stated:

The powdered examination gloves also fulfill the requirements of the performed product tests according to EN 455-1, 455-2, 455-3 as well as EN ISO 10993-5 and 10993-10, ASTM F1671 and EN 455-4, which demonstrates that the powdered latex gloves are in conformity with the relevant general safety and performance requirements of MDR 2017/745 (Annex I).

However, the analysis of the “medical background, current knowledge, state of the art” led to the conclusion that usage of powder for lubrication of gloves (making them easier to put on the hands) cannot be considered as state of the art. Usage of powder on gloves seems to present numerous risks to patients and health care workers, including inflammation, granulomas and respiratory allergic reactions (44) that cannot be corrected or eliminated by labeling or a change in labeling. Moreover, there are non-powdered alternatives that provide similar performance as the various powdered glove types do. Thus, the benefits of powdered gloves appear to only include greater ease of donning and doffing, decreased tackiness, and a degree of added comfort, which seems to be nominal when compared to risks posed by those products.

5. Recommended changes

affected	Changes or Tasks	Description
☒	Classification	On the DoC and in the technical file, the manufacturer currently specifies two rules that are used to classify the device. To ensure conformity, it is recommended to indicate only one rule for classifying the product.
☒	Clinical evaluation	The data of the proactive PMS and customer surveillance (starting in Q3 of 2020) should be included in the next update of the clinical evaluation
☒	Risk management	• Further aspects that should be considered in the risk analysis: ○ For individual use only ○ It is necessary to change the gloves in case of any defect, puncture, damage, contamination, etc. ○ Keep in dry condition and avoid the sunlight or other ozone sources ○ Keep away from insects It is recommended to extend the risk analysis by those aspects.
☐	PMS/PMCF	
☐	IFU	
☐	Application	
☐	Intended use	
☐	Patient population	
☐	Design of the product	
☐	Material	
☐	Packaging	
☐	Production process	
☐	Additional testing	
☐	Other	

6. Date of the next clinical evaluation report

The examination gloves (latex powder free and nitrile - powder free) are well established and do not carry significant risks. The data is sufficient to establish that the examination gloves (latex powder free and nitrile - powder free) perform as intended and are safe for the user and surrounding persons. Therefore, the clinical evaluation is actively updated every 3 years. However, in case Sri Trang Gloves (Thailand) Public Company Limited receives information from PMS that would influence the current evaluation, the update will be performed at that time.

7. Evaluators qualification

The clinical evaluation was conducted by an researcher that holds a bachelors and masters degree in biology and a research doctorate (Dr. rer. nat.) from the University of Veterinary Medicine Hanover, Germany. SML had been in scientific research at the Leibniz University Hannover and the University of Veterinary Medicine Hanover for more than 4 years. Hence, she has experience in the field of medical writing and the analysis of primary data. Furthermore, she has strong experience in the search and evaluation of data from various databases. She received continuing education in quality management, regulatory affairs and clinical evaluation report compilation in accordance with guidance document MEDDEV 2.7.1 as well as MDD and MDR. Thus, education and professional experiences qualify SML to objectively conduct this clinical evaluation.

The final version of the clinical evaluation was conducted by an researcher that holds a German university diploma in biology and a research doctorate (Dr. rer. nat.) from the TU Dresden, Germany. CGA had been in scientific research at the TU Dresden and BGD ECOSAX GmbH for nearly ten years. Hence, she has experience in the field of scientific writing and the analysis of primary data. Furthermore, she has strong experience in the search and evaluation of data from various databases. She received continuing education in quality management and became quality management representative. Furthermore, she received continuing education in regulatory affairs and clinical evaluation report compilation in accordance with guidance document MEDDEV 2.7.1 as well as MDD and MDR. Thus, education and professional experiences qualify CGA to conduct this clinical evaluation objectively.

8. Annex I

8.1. Documents provided by the manufacturer

For a complete list of all documents that were provided by the manufacturer for this clinical evaluation, see section 9 of the corresponding CEP dated 2020-09-02.

8.2. Literature

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