TO BE PRINTED ON HEADED PAPER

PARTICIPANT INFORMATION SHEET AND INFORMED CONSENT FORM FOR PARTICIPATION IN THE CLINICAL STUDY CODE CLI-05993AB1-06 "MiSTIC" study

Study Title:	A 26 week, randomized, double blind, multinational, multicentre, active controlled, 2-arm parallel group trial comparing CHF 5993 100/6/12.5 µg pMDI (fixed combination of extra fine formulation of beclometasone dipropionate plus formoterol fumarate plus glycopyrronium bromide) to CHF 1535 200/6 µg pMDI (fixed combination of extra fine formulation of beclometasone dipropionate plus formoterol fumarate) in subjects with asthma uncontrolled on medium doses of inhaled corticosteroids in combination with long-acting ß2-agonists (MiSTIC)
Short Study Title:	Step-up to Medium Strength Triple Therapy vs High Strength ICS/LABA in Adult Asthmatics Uncontrolled on Medium Strength ICS/LABA (MiSTIC)
Protocol No.:	CLI-05993AB1-06
Study Sponsor:	Chiesi Farmaceutici S.p.A., Via Palermo 26/A, 43122 Parma, Italy
Investigator name:	(to be completed)
Study Centre/Hospital name and address	(to be completed)
IRAS ID:	1004813
Participant No.:	

Invitation:

You are being invited to take part in a clinical research study sponsored by Chiesi Farmaceutici S.p.A. Before you decide whether or not to participate, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully, and if you wish, discuss it with your close relations or your general practitioner. Ask your Study Doctor if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part in the study.

Thank you for taking the time to read this Participant Information Sheet.

1. What is the purpose of the study?

The purpose of this study is to assess the efficacy (effectiveness) and safety of Trimbow® medium dose, compared with Foster® high dose, in participants with asthma. Your participation will help the sponsor to further understand which treatment works better in achieving specific goals in the management of your disease, including control of symptoms, quality of life, and prevention of disease worsening and side effects of the study drugs.

2. What are the drugs that are being tested?

CHF 5993 100/6/12.5 µg pMDI is a fixed combination of three active components:

- **beclometasone**, an inhaled corticosteroid (ICS) able to reduce the airway inflammation;
- 2 bronchodilators able to relax your muscles of the airways, keeping the airways open, with benefit on your breathing. Both belong to commonly used types of drugs, well established in the treatment of asthma:
    - **formoterol**, a “long-acting beta2 agonist” (LABA);
    - **glycopyrronium**, a “long-acting muscarinic antagonist” (LAMA).

Therefore, those three components are able to open up your airways and to reduce symptoms due to your asthma.

The drug has been developed by Chiesi Farmaceutici S.p.A and approved by the European Medicines Agency (EMA) in a spray (also called pressurised metered dose inhaler) for the treatment of asthma to improve lung function, health status and participant’s condition, to decrease symptoms, and to prevent deterioration/progression of asthma. The drug being launched on the market is called Trimbow® (code CHF 5993) and has been approved by the European Commission in January 2021 for maintenance treatment of asthma.

CHF 1535 pMDI is a combination of two of the above-mentioned components: **beclometasone** and **formoterol**. This drug has been approved for asthma with the name of Foster®, in Europe, in 2006 (medium dose: 100/6 µg) and in 2015 (high dose: 200/6 µg).

3. Why have I been asked to participate?

You are being invited to take part in this study because your asthma is not well controlled with your current asthma treatment, this means that despite the provided treatment you still show asthma symptoms like wheezing, cough, difficulty of breathing, and you need to use additional medicine to control the inflammation and to relieve the symptoms associated with your disease.

It is expected that approximately 1400 participants will be included in the study in about 200 sites in approximately 16 countries.

4. Do I have to take part?

No. It is up to you to decide whether to take part in the study. If you decide to take part, you will be given this Participant Information Sheet to keep and will be asked to sign the consent form. Your participation in the study is completely voluntary and you may decide to withdraw at any time without giving any reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

If you decide not to take part in this study, you will not receive any penalties or loss of usual benefits, and your Study Doctor will refer you to other alternative treatment available for your condition. Please consult the Study Doctor about your options as well as the risk and/or benefit of these alternative treatments.

5. What will happen if I take part?

This study will last 30 weeks (from the time you may sign the informed consent to the end of study). There are 7 visits in total.

At the first visit (Visit 0), the Study Doctor will fully explain the study procedures and give you the opportunity to ask any questions to clarify anything that may not be clear or that you don’t understand. If you agree to participate in this study, you will need to sign the Informed Consent Form. All your current medicines will also be reviewed and where applicable any changes in your medicines

and what you are not allowed to use will be discussed with you, in particular with respect to your asthma treatment. Some demographic data as age, sex, race and ethnic origins will be collected.

A card will be given to you with the Study centre/hospital address, telephone number of the Study Doctor to contact in case of emergency. You should always carry this card with you while you are involved in the study.

At the second visit (Visit 1, also called screening), your Study Doctor will check if you are suitable for participating in this study. You may be asked to stop some medications, the Study Doctor will provide further details. You will be given CHF 1535 medication (100/6 micrograms) to be used for the first 2 weeks of the study (run-in period) at the dose of 2 puffs twice a day (2 inhalations in the morning and 2 inhalations in the evening).

At the third visit (Visit 2, also called randomisation), if your medical condition is appropriate for the study, you will receive one of the two study treatments below, to be taken for 26 weeks (from Visit 2 to Visit 6):

- **Treatment A:** CHF 5993 100/6/12.5 micrograms (i.e. 100 micrograms of beclometasone dipropionate plus 6 micrograms of formoterol fumarate plus 12.5 micrograms of glycopyrronium bromide)

  or

- **Treatment B:** CHF 1535 200/6 micrograms (i.e. 200 micrograms of beclometasone dipropionate plus 6 micrograms of formoterol fumarate)

Whatever the treatment you have been assigned to, the dosing will be 2 puffs twice a day (2 inhalations in the morning and 2 inhalations in the evening). Both inhalers are pressurised metered aerosols. If you usually use a spacer (like Aerochamber Plus), you should continue to use it for the intake of the study medicines; a spacer will be assigned to you by you Study Doctor.

You will be randomly assigned to either treatment group A or B ("Randomly assigned" means that whatever treatment you get will be by chance, like flipping a coin or drawing names out of a hat.) You have an equal chance (50%) of being assigned to either treatment group. Participants in each group have different treatments and the responses to these different treatments will be compared.

Neither you nor your Study Doctor will know which one of the study treatments you are taking (double blind) until the study ends. All treatments are presented in an identical manner so you can't identify the treatment you are taking. Should it be necessary in the event of an emergency, your Study Doctor has the possibility to find out which treatment has been taken.

Throughout the study, you will be allowed to take salbutamol as rescue medication if you need it.

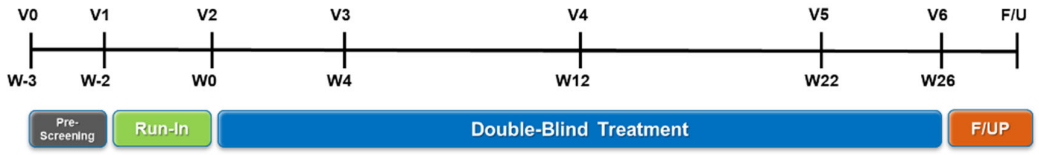
One week after the last treatment visit you will be contacted by phone for a final review of your health.

6. What do I have to do?

If you decide to participate, you will have to come to see your Study Doctor 6 times. You will be invited early in the morning and the assessments will start preferably at the same time for each of your visits. Visit 1 will last approximately 2 hours, visits 2 to 6 will last approximately 5 to 6 hours.

It may happen that additional visits are performed during the study at the discretion of your Study Doctor in order to check your asthma and your welfare.

The following scheme shows what your participation will involve up to the end of the study:



W: week; F/U: Follow-up

The section below describes the major tests and procedures that you will undergo. The different procedures for each visit are indicated in a table below.

Electrocardiogram (ECG) heart test
Your heart function will be monitored at visit 1 by a single ECG test before you take the study medication. The ECG does not hurt. You lie down or stay in resting position and have round sticky patches placed on your body. Wires go to the machine to measure how your heart is working.

Oscillometry
During the study, Oscillometry tests will be performed from Visit 2 to the end of the study. Measurements are made by a machine while you breathe normally and wear a nose clip. It will take few minutes and the machine will record information about your lungs.

FeNO test
At visit 2 and visit 6, you will be asked to blow into the FeNo device. You breath into the machine for few minutes. It measures specific characteristics of your airway inflammation.

Lung function test
This is like the “blowing” test that you usually do with your lung doctor (Pneumologist). You wear a nose clip and you can choose whether you stand or sit. The machine (the spirometer) will record the amount of air you are able to breathe in and out under medical supervision and instructions.
These blowing tests will be carried out at every visit.

At screening: as part of this test, a standard dose of salbutamol (a bronchodilator with rapid action) will be administered to you and then you will repeat the blowing test to see if it improves your lung function. This is a test to know whether you may participate to the study or not. Then at each visit (from Visit 2 to Visit 6) your lung function will be measured 45 and 15 minutes before taking the first dose of the day of the study medication and then 2 hours after taking the study medication.

Your Study Doctor will give you a portable spirometer device to test your lung function at home on a weekly basis in the morning. The test should be performed preferably on the same morning day of each week throughout the whole study period from Visit 1 to Visit 6. You will measure your lung function 45 and 15 minutes before taking the first dose of the day of the study medication and then 2 hours after taking the study medication. The device is linked to an application present on a smartphone device that will be also provided to you.

The Study Doctor will explain the use of the portable spirometer device and the associated smartphone to you carefully. **You will be asked to bring these devices to each visit to the hospital/clinic**.

Blood tests

At visit 1, you will have a blood test to find out if it is still safe for you to participate. You should not eat for at least 8 hours before the visit 1, this is what is called fasting conditions. At Visit 2 and Visit 6, a new blood test will be performed for Eosinophils evaluation. Your Study Doctor will take about 15-20 milliliters of your blood (about 3 teaspoons). Your blood will be sent to laboratory for analysis and after the analysis the samples will be destroyed.

If you are a woman and can become pregnant, the blood test at visit 1 will also check if you are pregnant or not. At all other visits, a simple urine test will be taken to confirm whether you are pregnant or not.

Urine and serum Biobanking

You will be asked to provide urine samples and additional whole blood samples of about 10 milliliters of blood (about 2 teaspoons) at baseline (Visit 2) and at the end of treatment (Visit 6 or early termination visit) before the study drug administration. These samples may later be used to study biological markers to help understand the biological effects and reasons for any different responses to the study drugs. The results and other information from these analyses will not be placed in your medical record and the anonymised data may be published. Samples will be processed and stored in the secure central laboratory:

Labcorp Central Laboratory Services Sàrl

7, rue Moïse-Marcinhes,

1217 Geneva, Meyrin

Switzerland

until the end of the trial. After that samples can be exported to a bioanalytical laboratory where they could be analyzed and/or kept stored for a maximum of 20 years.

Covid-19

Additional laboratory testing for COVID-19 may be done throughout the study. The COVID-19 testing results will be shared with you and if the results are positive all efforts will be made to keep you safely on the study treatment.

Electronic diary

Your Study Doctor will give you an electronic peak flow machine/e-diary which is a kind of portable machine to test your lung functions at home on a daily basis (in the morning and in the evening).

You will also need to answer some questions each morning and evening about your asthma symptoms, the frequency of night awakenings due to asthma and requiring rescue medication, the daily intake of your study medication and use of rescue medication.

The Study Doctor will explain the use of this machine to you carefully.

You will be asked to bring this machine to each visit to the hospital/clinic.

Questionnaires about quality of life and impact of asthma

During the study you will be asked to complete one or more questionnaires. The Study Doctor will check their completeness before you leave the centre:

- The **Asthma Control Questionnaire© (ACQ)** to assess the level of control of your asthma will be completed at Visit 1, Visit 2, Visit 4 and Visit 6.

- The **Asthma Quality of Life Questionnaire (AQLQ)** to measure the impact of your asthma on physical, emotional, social and occupational aspects of life will be completed at Visit 2, Visit 4 and Visit 6.

- Other questions about the impact of asthma in your daily activities (e.g. sick leave days from work, number of days spent at hospital due to asthma…).

The table below provides you a summary about the tests and procedures your will undergo during the study.

Visit	Initial visit	Screening	Treatment Period					FU
	V0	V1	V2	V3	V4	V5	V6/ETD*	
Time (Wks)	-3	-2	0	4	12	22	26	27
Discussion about the study	X							
Interview about health and treatments		X	X	X	X	X	X	X
Physical examination		X					X	
ACQ		X	X		X		X	
AQLQ			X		X		X	
Blood pressure		X					X	
ECG		X						
FeNO test			X				X	
Oscillometry			X	X	X	X	X	
Lung Function testing		X	X	X	X	X	X	
Blood test**		X	EOS				EOS	
Biobanking sample (blood and urine)			X				X	
Pregnancy test		X	X	X	X	X	X	
Training on e-diary/e-peak flow meter use and on recognition of developing asthma exacerbation		X	X					
Home spirometry		X (once weekly in the morning)						
e-diary completion and home PEF***		X (daily am/pm)						
eDiary review			X	X	X	X	X	
Study medication		◄———					———►	

*ETD: Early Treatment Discontinuation

**EOS: Eosinophils evaluation

***PEF: Peak Expiratory Flow measurement

The procedures described for Visit 6 will also be done in case your Study Doctor decides to stop your participation to the study prematurely. In case you stop the study prematurely, your Study Doctor will discuss with you to know would be willing to continue with the study visits, e-diary and e-peak flow while no longer taking either of the study treatment. If you accept, you will continue attending study visits according to the study visit schedule: the same tests will be done at each visit as described in the table and you should continue to complete diary data/Home PEF. Urine pregnancy tests will be performed at study visits in all women of childbearing potential.

During the course of the study, you may not be allowed to take the medicine(s) you normally take for your asthma. Your Study Doctor will discuss with you if they are permitted. Ongoing medication you take for other conditions must be checked by the Study Doctor and, if permitted, the dosage should be kept as constant as possible throughout the study.

Rescue medication (salbutamol) is permitted throughout the study as needed but you will be asked to follow carefully the maximum inhalations allowed and where possible, avoid taking them for at least 6 hours prior to the hospital/clinic study visits.

Oral contraceptives, if taken, should be continued throughout the study (for females of childbearing potential).

Once the study is complete, there will be no provision for study drug to be continued to be provided.

A final report will be written at the end of the study. The study doctors will be able to share the results of the study with the participants once the report is available, should you request this.

7. What are the possible benefits of taking part?

There might be benefits for you in participating in this study. If you are found suitable to participate, it means that your asthma is not currently ideally controlled and depending on the treatment assigned to you, your symptoms are likely to improve.

More importantly, your disease and overall condition will be carefully and closely evaluated by the Study Doctor. This will help the Study Doctor to assign you a more suitable drug therapy when the study is over (either by changing the dose of the drugs you were taking previously or by adding additional drug(s))

We cannot promise that the study will help you but the information we get could help treat people with asthma with better medicines in the future.

8. What are the possible disadvantages of taking part?

It might happen that you do not get any benefit from the study and that the study treatments assigned to you will not improve your asthma and that your symptoms will remain the same as the ones before the study entry, or even worsen. If that is the case, you can take rescue medication to relieve symptoms and you can end your participation whenever you want. Your participation will also mean that you will see your Study Doctor regularly, he/she will be able to check your conditions and ensure your safety during the study.

9. What are the side effects of the study drugs or of the study tests?

All medicinal products have known or unforeseeable side effects. The probabilities of side effects are defined as follows: very common (>10%), common (1-10%), uncommon (0.1-1%), rare (0.01-0.1%) and very rare (<0.01%), unknown (probability cannot be evaluated with available data).

The drugs tested are combination of two or three of these active components: beclometasone, formoterol and glycopyrronium. The side effects that may occur are those known for the same combinations already on the market, i.e. Foster® and Trimbow®.

The side effects known to be related to the use of the combination of **beclometasone plus formoterol** (Foster®) or any of the single substances are listed below:

- **Common**: Pharyngitis (sore throat), oral candidiasis (fungal infection of oral cavity), headache and voice alteration.
- **Uncommon**: Influenza (common flu), fungal infection of throat and food pipe, gastroenteritis, inflammation of the sinuses, itchy, runny or blocked nose, fungal infections of the vagina, decrease in white blood cells and potassium, skin allergy, increase in blood sugar, restlessness, trembling, dizziness, inflammation of the ear, palpitations (heartbeats that suddenly become more noticeable), changes in the electrocardiogram (heart trace), unusual fast or irregular heartbeat, disorders of heart rhythm, increased blood flow to some tissues in the body, reddening of the face, cough, productive cough, throat irritation, asthma attack, redness of the pharynx, diarrhea, dry mouth, upset stomach, difficulty swallowing, burning sensation of the lips, nausea, altered taste sensation, skin itching, increased sweating,

redness of skin, muscle cramps and pain in muscles, alterations of some constituents of the blood like increase in C-Reactive protein, in the number of blood platelets, in free fatty acids ,in the blood level insulin, and in blood ketone and decrease of the blood level of cortisol, increase of blood pressure.

- **Rare**: Extra heart beats, angina pectoris (chest pain due to underlying ischemic heart disease), narrowing of bronchus (due to bronchodilator response), swelling of subcutaneous tissues, nephritis (inflammation of nephrons in kidney) and decrease in blood pressure.
- **Very rare**: Fall in the number of blood platelets, decreased bone density, hypersensitivity reactions, including erythema, lips, face, eye and pharyngeal oedema, adrenal suppression, cataract (clouding of eye lens), glaucoma (increased pressure leading to damage of optic nerve), difficulty breathing, worsening of asthma, growth retardation in children and adolescents, peripheral oedema (swelling of hands and feet), increased pressure in eyes.
- **Not known**: Psychomotor hyperactivity, sleep disorders, anxiety, depression, aggression, behavioural changes (predominantly in children), blurred vision.

The side effects mentioned above apply also for CHF 5993 (Trimbow®)**,** that contains **beclometasone plus formoterol plus glycopyrronium**. Additional side effects have been reported for CHF 5993 and are listed below:

- **Common**: urinary tract infection, runny or stuffy nose and sneezing (nasopharyngitis).
- **Uncommon**: abnormal or reduced sense of taste, numbness, cough and productive cough, nose bleeds, tooth decay, mouth inflammation (stomatitis), pain in arms or legs, pain in muscles, bones or joints of the chest, fatigue.
- **Rare**: fungal infections of the chest, hypersensitivity reactions including erythema, lips, face, eye and pharyngeal oedema, decreased appetite, sleep disorders (sleeping too little or too long), unusually slow heartbeats, leakage of blood from a vessel into the tissues surrounding it, asthma exacerbation, pain in the back of the mouth and throat , dry throat, painful and frequent urination, difficulty and pain when passing urine, fatigue, increase in blood pressure.

Inhalation of high doses of corticosteroids (like beclometasone) for prolonged periods may cause systemic effects. These include: depression of adrenal function, delayed growth in children and adolescents, reduced bone mineral density (thinning of the bones), eye diseases such as cataract (opacity of lens) and glaucoma (increased pressure in the eye, causing poor night vision, blind spots, and loss of vision to either side), sleeping problems, depression or feeling worried, restless, nervous, over-excited or irritated (these events are more likely to occur in children but the frequency is unknown). Systemic side effects are however extremely improbable with the recommended doses.

As with other inhalation therapy, paradoxical bronchospasm (a difficulty in breathing caused by a sudden constriction of the muscles in the walls of the bronchioles) may occur.

There is a potential risk of unforeseeable allergic reactions as for any drugs. Hypersensitivity reactions like skin allergies, skin itching, skin rash, reddening of the skin, swelling of the skin or mucous membranes especially of the eyes, face, lips and throat may occur.

In addition, as for any drugs, there may be unforeseeable risks that we currently do not know about. You will be given any new information that may affect your willingness to start or continue in the study.

In case you have to use the rescue medication (salbutamol), you may possibly experience side effects associated with this drug: the most common are headache, tremor and increased heart rate and occasionally, muscle cramps, mouth and throat irritation and palpitations. Fall in the blood level of potassium and increased blood flow to the extremities (peripheral dilatation) may also occur.

You may also experience some side effects with the study tests you will undergo.

You may experience minor discomfort from the blood sampling procedures, and occasionally some bruising or inflammation of the veins used can occur. These effects normally disappear within a few days.

The ECG pads that are placed on your chest to monitor your heart occasionally may irritate your skin and cause itching and redness. The redness resolves quite quickly. Please note; it may be required to clip/shave small areas of hair where the ECG pads stick to your chest.

If you experience any side effects, you should write them down and report them to your Study Doctor at your next contact. If you should in any way become concerned, or in case of emergency, you should contact immediately the Study Doctor/study staff at the telephone numbers reported on the first page of this "Participant Information Sheet".

If some side effects are still ongoing when the study ends, the Study Doctor may contact you to get the status of these side effects.

Pregnancy Risks

If you are a woman, there may be unknown risks to the foetus (unborn child). If you are a female participant of childbearing potential, you must not be pregnant and must not intend to become pregnant during the whole study period and therefore use a reliable method of contraception. Your Study Doctor will discuss with you in that case.

Acceptable safe contraception includes:

- Placement of an intrauterine device (IUD) or intrauterine hormone-release system (IUS).
- Combined (oestrogen and progesterone containing) hormonal contraception associated with inhibition of ovulation (oral, intravaginal, transdermal)
- Progesterone-only hormonal contraception associated with inhibition of ovulation (oral, injectable, implantable)
- Bilateral tubal occlusion
- Vasectomised partner
- Sexual abstinence

At the first visit a pregnancy test is to be carried out if you are a woman of a fertile age. Breast-feeding women are also not allowed to participate in this study, because the study drug may enter the child's body through the breast milk and cause harm.

If you should become pregnant despite precautions during the study period, please contact your Study Doctor instantly, who will withdraw you immediately from the study. For safety purposes, we would like to keep following you until the end of the pregnancy and till the age of one year of the child to find out if the study medicine has affected your child.

A separate and specific Informed Consent will be signed by you (and your partner if required according to local laws) if you accept participating in this follow up.

If you are a man and your partner became pregnant during your participation in the study, you must immediately inform the Study Doctor. There is no need to recommend specific contraceptive methods, since it is not expected that there could be any risk for the foetus via paternal transmission. However, for safety purposes, we would like to keep following your partner's pregnancy until the end and till the age of one year of the child to find out if the study medicine affected your child. A separate and specific Informed Consent will be signed by you (and your partner if required according to local laws) if you accept participating in this follow up.

10. What will happen to any sample I give?

All samples (including urine and blood) will be collected at the hospital/clinic by the Study Doctor or the research nurse and will be processed in the secure central laboratory:

Labcorp Central Laboratory Services Sàrl

7, rue Moïse-Marcinhes,

1217 Geneva, Meyrin

Switzerland

until the end of the study. Urine and blood samples for biobanking can be exported to a bioanalytical laboratory where they could be analyzed and/or kept stored for a maximum of 20 years. All other samples will only be used for the purpose of this study and will be destroyed as soon as they are no longer needed.

Samples will only be identified by the study number and your participant number.

If you withdraw your consent for participation in the study, we will need to use the data collected up to your withdrawal. Any sample (e.g. blood/urine) already collected and sent off site for analysis may still be analysed and reported, unless you ask for them to be destroyed following your withdrawal.

11. What if new information becomes available?

If any important new information is found during the study that may affect your willingness to carry on taking part in the study, the Study Doctor will share this information with you. If you decide to continue in the study you may be asked to sign a new consent form. If you decide not to carry on, your study doctor will make arrangements for your care to continue.

12. What happens when the clinical study stops?

Your participation in the study may be stopped for any of the following reasons:

- Failure to comply with the Study Doctor's instructions;
- The Study Doctor decides it is in the best interest of your health and welfare to discontinue;
- The sponsor may stop the study or the development of the investigational drug.

In any case, your Study Doctor will refer you to other alternative treatments available for your condition.

13. Does the study have insurance cover?

The present study is covered by an insurance contract held by the Sponsor, Chiesi Farmaceutici S.p.A.

14. Are there any costs or compensation for my participation in the study?

The study drug will be provided to you for free. All costs for examination, assessments, laboratory testing, and study medications are paid by the sponsor of this study.

A payment of up to £750.00 will be made on completion of the study for your time and to compensate for any inconvenience. If any repeat visits are required e.g. for extra blood samples you will be paid for the visit(s). In addition, we will reimburse you any reasonable costs you might have associated with your travel to the study site.

If you are enrolled onto the study but withdraw prior to completion, you will be paid on a pro-rata basis. You should be aware that data collected up to the point at which you have withdrawn from the study may be used.

If you are screened for the study but are found to be unsuitable, or you attend the unit and are not dosed, you will receive a pro-rata compensation payment.

The payment will be made via <please select the appropriate method from the following:
Cash payment / a BACS payment, made directly into your account / Cheque*.
*Please bring your bank details with you to the consent visit.>

You are responsible for paying tax on this payment if this is appropriate to your circumstances. If you receive a means-tested benefit of any kind, you should check whether participating in this study will have any effects on the benefits you receive. You should inform your insurance company that you are taking part in this study if you have private medical insurance.

Medical research may result in new products, tests, or discoveries. These may have value to others, but you will not share in any financial benefits from these products, tests, or discoveries.

The study centre/hospital will receive remuneration for conducting the study.

Compensation for Injury

If you suffer any side effect or injury, notify your Study Doctor immediately so that you can receive appropriate medical treatment.

If you suffer any side effect or other physical injury resulting directly from the clinical investigation procedures, the Sponsor will pay for the reasonable costs of medical treatment to the extent permitted by the law of Great Britain according to Association of the British Pharmaceutical Industry (ABPI) if:

- Your injury was not deliberately caused
- The clinical investigation doctor was immediately notified about your injury; and
- The medical advice of the clinical investigation doctor was followed

The Sponsor has insurance to cover clinical investigation-related injuries. If any injury is caused by your participation in the clinical investigation, the Sponsor will compensate you in accordance with the law of Great Britain.

15. What are my responsibilities from participation in this study?

If you decide to participate in this study, you will have to follow certain rules.

- You must comply with all instructions provided during participation in this study. In case of uncertainty about what to do, or if you are unable, in any way, to follow the study procedures, please contact your Study Doctor.
- You and your partner must comply with the method(s) of contraception indicated by the Study Doctor in order avoid a pregnancy during your participation in the study.
- It is very important that you communicate all the information to the Study Doctor in your possession on your health and on the medications, you are taking or which could you start taking over the period of the study. These include over-the-counter medicines, vitamins and supplements. If the Study Doctor is not made aware of all this information, you could jeopardise your health.
- Notify the Study Doctor if you feel at all unwell, at any time during the study. If this occurs while you are not in the Study Centre/Hospital, you must make every effort to contact the Study Doctor (his/her name and contact number will be provided on a card for you to keep for the duration of the study and are detailed within this document also).

We would like to remind you that compliance with the instructions given to you for this study is very important to ensure your health and that of the people around you.

16. Will my taking part in the study be kept confidential?

Taking part in this study will remain confidential. You will be identified by a patient number. Your medical data will be computerised and will be transmitted only to Chiesi and designated representatives for the purpose of analysing the results.

The Sponsor is responsible for your personal data confidentiality and agrees to abide by the data protection laws by taking specific personal data protection measures, by assuring your identification by study number. All information which is collected about you in records that leave the doctor's office for the purposes of medical, laboratory, statistical or regulatory activities related to the study research will be identified by your study patient number. Your full name or any address details and telephone number will not be included in these records. You have the right to request updated information about what data is recorded and you have the right to request corrections. Chiesi will share the study results with qualified medical researchers.

A description of this clinical study will be available on http://www.encepp.eu/encepp/studiesDatabase.jsp. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Coding of your data

Your personally identifiable information and health information collected in this study will be labelled with a unique code number. The code number will be used in place of your name and other information that directly and easily identifies you. Only the study site will have the link between your personal information and the coded data. This link will not be provided to the sponsor; only your coded data will be sent to the sponsor. The sponsor will take measures to protect the confidentiality and security of your coded data and their privacy in accordance with current law.

Some of your information will be sent outside of the United Kingdom. Other Countries must follow UK rules about keeping your information safe.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

Personal Data

By signing the consent form to take part in this study, you agree for the Study Centre to collect and process your personal information and agree for Chiesi Farmaceutici S.p.A., who is the Sponsor for this study, to use your personal data as described in this document for the study purposes, i.e. learn about the study drug, support approval of the study drug by health authorities, support future research and to improve science.

Please be aware that providing your personal data is mandatory in order to evaluate your eligibility for the enrolment and to include you in the study. The refusal to give the requested consent to process your personal data will imply the exclusion from the study.

Which personal data will be collected?

The Study Centre and Chiesi Farmaceutici S.p.A. will process your personal data as Data Controllers. With regard to data about you that is collected as part of this study, a fundamental distinction is made between:

1. the personal data from which you can be directly identified (e.g. name, year of birth, address, including your sensitive data, such as medical history, patient's medical condition, blood samples, etc.) (Un-coded Data);
2. pseudonymised data, where all information that might enable conclusions as to your identity to be drawn is replaced with a code (Coded Data).

3. anonymised data, for which it is no longer possible to trace it back to you.

Who will have access to your personal data?

Only the Study Doctor/Study Centre's staff will have access to Un-Coded Data. Any transfer of data outside the Study Centre, in particular to the Sponsor, takes place only in the form of Coded Data. However, other delegated people may also need to look into Un-Coded Data to ensure that the study is being conducted properly in accordance with laws and ethical requirements, including:

- People authorised by the Sponsor such as monitors and auditors;
- People from regulatory authorities overseeing the study.

Each of these individuals will be obligated to protect the confidentiality of your personal data and to use and disclose it only as described in this document. Your personal data is protected against unauthorised access.

How will your Coded Data be shared and transferred?

The Sponsor may share your Coded Data with other companies within its group, with its service providers, its contractors, current and future commercial partners and with other research institutions who will use your Coded Data only for the purposes described above.

Furthermore, your Coded Data might be retained, used and processed outside the purpose of this study exclusively for legitimate scientific reasons.

Your data in anonymous form might be communicated and shared with third parties, such as qualified medical researchers, exclusively for legitimate scientific reasons.

Some of the above mentioned third parties may be established in countries outside the European Union that may not guarantee an adequate level of protection of personal data: in this case the Sponsor takes appropriate steps to ensure that the transfer complies with local and applicable data protection laws.

On which grounds do you process your personal data?

Your data will be processed according to the following legal grounds:

- Your consent as expressed in this Participant Information Sheet,
- Sponsor legitimate interest, (for example in case you withdraw from the study, the Sponsor will keep processing the data about you collected up to that time based on its legitimate interest).

How long will my personal data be stored?

Your personal data will be retained as necessary to perform the contractual and legal obligations arising out of the study, for a period up to 25 years after the end of the research study.

In addition, the Sponsor will retain your Coded Data for the data retention period identified in the standards of Good Clinical Practice, whatever the longest.

What rights do I have concerning my personal data?

The rights granted by the GDPR such as rights to access, change or move the information about you are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained based on the Sponsor's legitimate interest. To safeguard your rights, we will use the minimum personally-identifiable information possible.

Please note that you have always the right to lodge a complaint with a supervisory authority in case of unlawful processing of personal data.

If you have any questions concerning the handling of your personal data and you want to exercise the above-mentioned rights you should contact in the first instance the Study Doctor at the Study Centre, who can be contacted at: (insert)

You can also exercise the above-mentioned rights without formalities by writing to the Sponsor's DPO, whose details are available on the website www.chiesi.com and can be contacted at the following address dpoit@chiesi.com.

However, since your data is coded, the Sponsor is unable to identify and link data to a specific subject. Please be aware that when you contact the Sponsor you are sharing your personal information, so it is recommended that you always contact the Sponsor via the Study Doctor.

Please note that if you withdraw from the study, no new information referring to you will be further collected or added to the existing data, to the use of that already collected to determine, without alteration, the results of the study.

17. What will happen to the results of the research study?

A description of this clinical trial will be available on http://www.ClinicalTrials.gov. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time. In this website the current clinical study is identified by the study code: NCT05018598.

The results of the study will be presented to the Health Authorities or may be presented at scientific meetings. Your identity will not be revealed in any report or publication. You can ask your doctor to inform you about the study results.

A summary of the clinical study results will be also registered in the EU clinical study database and available at the following link https://www.clinicaltrialsregister.eu

In addition, the results of the study may be used to apply for marketing approval from Health Authorities for study drug; CHF5993 may be presented at scientific meetings.

18. Who is organizing and funding the research?

The pharmaceutical company Chiesi Farmaceutici S.p.A., Via Palermo 26/A, 43122 Parma (Italy) is sponsoring the study

19. Who has reviewed the study?

All research studies are reviewed by an independent group of people, called a research ethics committee to protect your safety, rights, well-being and dignity. This study has been reviewed and has been given a favourable opinion by [Research Ethics Committee Name].

This committee reviews research studies to protect the rights and well-being of the patients taking part. The approval from the [Research Ethics Committee Name] should not be thought of as an encouragement for you to take part in this study.

20. Involvement of your General Practitioner/Family doctor (GP)

Your study doctor will tell your family doctor about you taking part in the study and may ask them for medical information about you.

21. Contact for further information:

If you need further information or should you experience any illness, symptom or discomfort at any time during the study, please contact:

Main Study Doctor		
Other Study Doctor		
Study Nurse		

Contact(s) for questions about your rights
INSERT PALS Details for affiliated NHS Hospital
Name of Contact Person: <NAME>
Telephone Number: <NUMBER>
Address: <ADDRESS>

You can also contact the study centre/hospital independent advisor
<Insert contact details>
Name of Contact Person: <NAME>
Telephone Number: <NUMBER>
Address:<ADDRESS>

INFORMED CONSENT FORM

FOR PARTICIPATION IN THE CLINICAL STUDY CODE CLI-05993AB1-06

"MiSTIC" study

Study Title:	A 26 week, randomized, double blind, multinational, multicentre, active controlled, 2-arm parallel group trial comparing CHF 5993 100/6/12.5 µg pMDI (fixed combination of extra fine formulation of beclometasone dipropionate plus formoterol fumarate plus glycopyrronium bromide) to CHF 1535 200/6 µg pMDI (fixed combination of extra fine formulation of beclometasone dipropionate plus formoterol fumarate) in subjects with asthma uncontrolled on medium doses of inhaled corticosteroids in combination with long-acting ß2-agonists (MiSTIC)
Short Study Title:	Step-up to Medium Strength Triple Therapy vs High Strength ICS/LABA in Adult Asthmatics Uncontrolled on Medium Strength ICS/LABA (MiSTIC)
Protocol No.:	CLI-05993AB1-06
Study Sponsor:	Chiesi Farmaceutici S.p.A., Via Palermo 26/A, 43122 Parma, Italy
Investigator name:	(to be completed)
Study Centre/Hospital name and address	(to be completed)
IRAS ID:	1004813
Participant No.:	

	Please read the following statements and put your initials in each box to show that you have read and understood them and that you agree with them.	**Initials**
1.	I confirm that I have read and understood the Participant Information Sheet, and have been given the opportunity to ask questions and discuss this study. I have received satisfactory answers to my questions. I have been informed that I will receive a copy of this information sheet and signed consent form to keep for myself.	
2.	I voluntarily agree to participate in the above study, which is being conducted on behalf of Chiesi Farmaceutici S.p.A. (who is the Sponsor of this study). The study doctor has explained the nature and purpose of the study to me.	
3.	I understand my personal information including my full date of birth and race and ethnicity to be collected and used as part of this study and to be: • identified only with their patient ID number; • reviewed, processed and disclosed by and to the Sponsor and its authorised representatives and study monitors for the purposes described in the study protocol; • reviewed or audited by the appropriately authorised organizations; • published and sent to regulatory authorities in my country or other countries; and • transferred, if required, to any country, where laws protecting my personal information may be different to my own.	

4.	It has been explained to me that the procedures being tested in this study may involve risks to me which are currently unforeseeable.	
5.	I understand that the Study Doctor will inform me in case of further analyses, not foreseen at this stage, planned on my biological samples, and a new consent form will be submitted to my attention.	
6.	I understand the importance of not becoming pregnant during the study. I agree to comply with the instructions outlined for this study and I will inform the Study Doctor if there is any risk of me becoming pregnant during the study (female participant) or if my partner becomes pregnant during the study (male participants).	
7.	I understand that I may request to see any data stored with regard to myself and request any errors to be corrected. I consent to the archiving of coded information (and documents inrelation to my participation in this study) and to its transmission outside the EuropeanUnion (if applicable). I consent to my confidential personal information, in anonymous form, being made available to qualified medical researchers conducting legitimate scientific researches.	
8.	I understand by having signed this consent form, it does not imply I have to participatein this study and I can withdraw at any time without giving a reason, and without affecting my future care. In case of withdrawn consent, no new information will be collected or added to existing data.	
9.	I understand that my urine and blood samples could be stored for up to 20 years to perform post-hoc biomarker analysis	
10.	I agree if my study doctor is not my family doctor, my family doctor will be told about me taking part in this study and asked for medical information about me.	
11.	I consent to my personal data being made available with direct access to people authorised by the Sponsor (Chiesi Farmaceutici S.p.A.) such as monitors and auditors, and people from regulatory authorities.	

PRINT PARTICIPANT'S SURNAME – FIRST NAME _____

Date: |__|__|/|__|__|/|__|__| **Signature**: _____

DD MM YY

_____ _____

SIGNATURE OF AUTHORISED REPRESENTATIVE
(IF APPLICABLE)

DATE OF SIGNATURE

I, the undersigned, Prof./Dr. _____ (Investigator name and surname), declare that I have explained the nature, goal, and risks of this clinical study, and that I have thoroughly and comprehensively answered all the questions asked by the participant, and that I have not attempted to influence or coerce the participant in any form in order to induce him/her to participate in the clinical study.

Date |__|__|/|__|__|/|__|__| **Signature**: _____ DD
MM YY

Produced in two copies (one to be given to participant and one for the Study Doctor)