**INFORMATION ACCOMPANYING INFORMED CONSENT FOR AUTHORIZATION OF THE COLLECTION AND FREEZING OF SAMPLES FOR THE BIOLOGICAL SAMPLES BANK AND PRESENT AND FUTURE RELATED GENETIC AND MINIMAL RESIDUAL DISEASE STUDIES.**

**Randomized, national, open-label, multicenter, phase III trial studying induction therapy with bortezomib/lenalidomide/dexamethasone (VRD-GEM), followed by high-dose chemotherapy with melphalan-200 versus busulfan-melphalan (BUMEL), and consolidation with VRD in patients under 65 years old with newly-diagnosed multiple myeloma.**

**Protocol code: *GEM2012MENOS65***

Before treatment begins, your doctor will talk to you about the need to obtain one or more samples of the cells that cause the disease for diagnostic purposes. These samples will be taken from the same blood collections and bone marrow aspirates that will be performed throughout the study.

The genetic study samples and other biological samples collected from patients will not be kept by the sponsor indefinitely. Use of the samples will be limited exclusively to monitoring minimal residual disease (study which indicates the risk of disease relapse) in patients and will be stored for this purpose, as long as the consent given by you is not revoked.

With respect to response to treatment, duration of the response and survival, genetic alterations observed in myeloma cells at the time of diagnosis and the amount of disease that remains after each stage of treatment—known as minimal residual disease--are extremely important. Samples will be analyzed centrally at one of the following four hospitals to ensure that the genetic studies, and those performed to determine minimal residual disease, are not only highly reliable, but homogenous across all study participants: *Hospital Clínico Universitario de Salamanca*, *Hospital Doce de Octubre* and *Hospital la Fe de Valencia*, and at the *Centro de Investigaciones Médicas Aplicadas (CIMA)* (Center for Applied Medical Research) in Pamplona. Thus, one of the tests that will be carried out is for the possible presence of changes in the chromosomes of your disease cells. In addition to tests for minimal residual disease, analyses of possible complications resulting from the treatment may also be done, complications which include hypothetical new cancerous tumors, in which case it may be necessary to collect additional samples. These tests will help determine the extent of disease reduction and therefore whether there is a greater or lesser risk of relapse.

Any genetic markers that can provide relevant prognostic data with respect to the disease and treatment given will be chosen as genetic study material. You should also be aware that a scientific need to study specific genetic markers may arise during the study or at a later time, but will always be related exclusively to your disease and/or the treatment you have received. However, if the intended study could be viewed as differing from the objectives set out in this document, we guarantee that we will approach you through your doctors to obtain new express consent from you, and thereby ensure that you have no doubts or issues with said study. If these tests should produce new information relevant to your health, this will be communicated to you and/or your immediate family for your benefit, unless you express in writing that you do not wish to be informed, or for this information to be communicated to your family. Anonymous data obtained from the genetic test will be public and/or can be consulted by investigators in the group, regulatory bodies and/or competent health authorities, which will allow for greater scientific knowledge of your disease and the treatments used. This is the major, overall benefit expected from these studies, and it is possible that the knowledge of certain specific information related to your case may benefit you directly.

So that we are able to freely handle the biological samples obtained from you to carry out these more sophisticated genetic tests, you will need to state that you have no objections, and therefore provide written consent for these studies to be carried out, which do not strictly correspond with the basic, standard diagnostic techniques.
The express consent we request will include permission to extract, use and store blood and marrow

samples, frozen at a very low temperature, for a period of at least five years at one of the following institutions: Centro de Investigación del Cáncer de Salamanca (*Salamanca Cancer Research Centre*,) Instituto de Investigación del Hospital Universitario 12 de Octubre *(Hospital Universitario 12 de Octubre Research Institute)* or the Servicio de Hematología del Hospital Universitario La Fe *(Hospital Universitario La Fe Hematology Division)*, or the *Centro de Investigaciones Médicas Aplicadas (CIMA)* in Pamplona. The managers of the hematology labs and cancer genetics research departments of these institutions will oversee this process, with an end to using them in novel genetic studies with similar objectives that may be carried out in future. The results from these studies will be handled in a strictly scientific manner, in the interest of more detailed information about your specific disease. You should know however, that you can demand that the samples you have donated be destroyed or irrevocably unlinked from your identity at any time. You will not need to specify the reason for this request as this is your legal right. Should you choose to have the samples destroyed or unlinked you should inform your study physician. However, you should also know that if you do exercise this right, you will no longer directly benefit from the information relevant to your health that may hypothetically be obtained from studies on this biological material. As well, please note that any samples that have not been irrevocably linked from you will be destroyed when all of the research objectives have been met and in accordance with legally established timeframes.

Under no circumstances will the samples and/or their analysis ever be used for commercial purposes, either by sale of the material to third parties or sale of the rights to perform studies on the samples. Please be advised that even if you choose not to authorize the collection, storage and use of your samples for the proposed studies, you can continue to participate in the study.

If the analyses are carried out, the results will remain confidential and will not be revealed to you or any other person outside of the study unless you or your legally authorized family members explicitly request this. On the other hand, your personal information from the aforementioned study will remain strictly confidential and the samples duly anonymized, linked only to an order code (made up of different digits that refer to the trial site and when you enrolled in the study) and sample ID number.

This investigational study has been reviewed and approved by your hospital's Ethics Committee. Any questions or concerns you may have can and should be addressed with your study physician, Dr. _____. You can also call the following number _____.

I, in agreement with all that is expressed herein, consider myself adequately informed and agree to having my blood and bone marrow samples collected, stored and used for possible complementary genetic studies now and in the future related to my disease and/or the treatment I receive.

Name_____Signature_____Date_____

## WRITTEN INFORMED CONSENT FORM

**Randomized, national, open-label, multicenter, phase III trial studying induction therapy with bortezomib/lenalidomide/dexamethasone (VRD-GEM), followed by high-dose chemotherapy with melphalan-200 versus busulfan-melphalan (BUMEL), and consolidation with VRD in patients under 65 years old with newly-diagnosed, multiple myeloma.**

**Protocol code: *GEM2012MENOS65***

I, (full name), _____

I have had the opportunity to ask questions about the study.

I have received adequate information about the study.

I have read the information sheet that was given to me.

I have spoken to Dr. _____

I understand that my participation in this study is voluntary.

I understand that I may with withdraw from the study:

1. At any time;
2. Without having to give an explanation
3. Without this affecting my medical care

By signing this consent form, I voluntarily agree to participate in this clinic trail and I authorize the use of all information obtained from it, including from possible complementary genetic studies related to my disease. I understand that I will receive a signed copy of this written informed consent form.

_____ _____

Signature of the Patient Date

_____ _____

Name and signature of the Investigator Date

## VERBAL INFORMED CONSENT IN THE PRESENCE OF WITNESSES

**Randomized, national, open-label, multicenter, phase III trial studying induction therapy with bortezomib/lenalidomide/dexamethasone (VRD-GEM), followed by high-dose chemotherapy with melphalan-200 vs. busulfan-melphalan (BUMEL), and consolidation with VRD in patients under 65 years old with newly-diagnosed, multiple myeloma.**

**Protocol code: *GEM2012MENOS65***

I, (full name), _____

state, under my sole responsibility, that (name of the patient participating in the trial): _____

Has had the opportunity to ask questions about the study.

Has received adequate information about the study.

Has read the information sheet provided to him/her.

Has spoken with Dr._____

Understands that his/her participation is voluntary.

Understands that she/he may withdraw from the study:

1. At any time
2. Without having to give an explanation
3. Without this affecting his/her medical care

_____ _____

Signature of the Witness Date

_____ _____

Name and signature of the Investigator Date

## INFORMED CONSENT BY A LEGAL REPRESENTATIVE

**Randomized, national, open-label, multicenter, phase III trial studying induction therapy with bortezomib/Lenalidomide/dexamethasone (VRD-GEM), followed by high-dose chemotherapy with melphalan-200 versus busulfan-melphalan (BUMEL), and consolidation with VRD in patients under 65 years old with newly-diagnosed multiple myeloma.**

**Protocol code: *GEM2012MENOS65***

I, (full name), _____

In my capacity as the: (relationship to the patient) _____ of (name of the participant) _____

I have read the information sheet that was given to me

I have had the opportunity to ask questions about the study.

I have received satisfactory answers

I have received adequate information about the study.

I have spoken with Dr. _____

I understand that his/her participation is voluntary.

I understand that she/he can withdraw from the study:

1. At any time
2. Without having to give an explanation
3. Without this affecting his/her medical care

(Name of the patient) _____ has received all relevant information about the study in my presence, adapted to his/her level of understanding. S/he has been informed that only data from his/her medical records that are related to the study will be verified by third parties, and agrees to participate in the study. By signing this form, I give my consent in order that said person may participate in this study.

_____ _____

Signature of the Representative Date

_____ _____

Signature of the Investigator Date