Practical experience in implementing surveillance of antiviral resistance in several European countries in accordance with personal data regulation

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Antiviral drug resistance: Viral Hepatitis

Hepatitis B

(PEG-) Interferon alpha
Nucleos(t)ides
Combination therapies

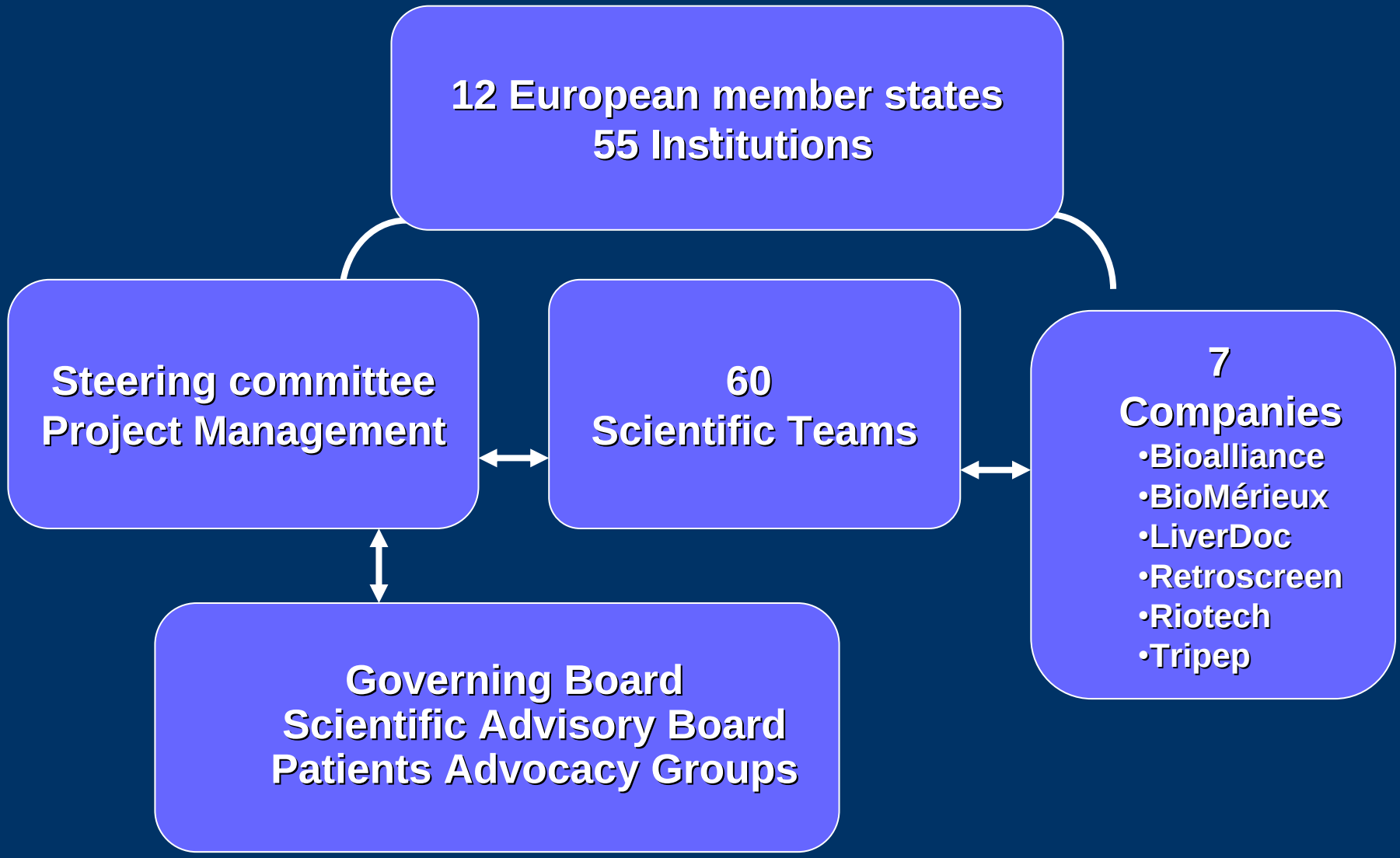
Hepatitis C

PEG-Interferon alpha + Ribavirin
New antivirals
(Enzyme inhibitors, etc.)

VIRGIL – European Network of Excellence integrating the expertise of national networks

+ ISRAEL

VIRGIL Network Composition



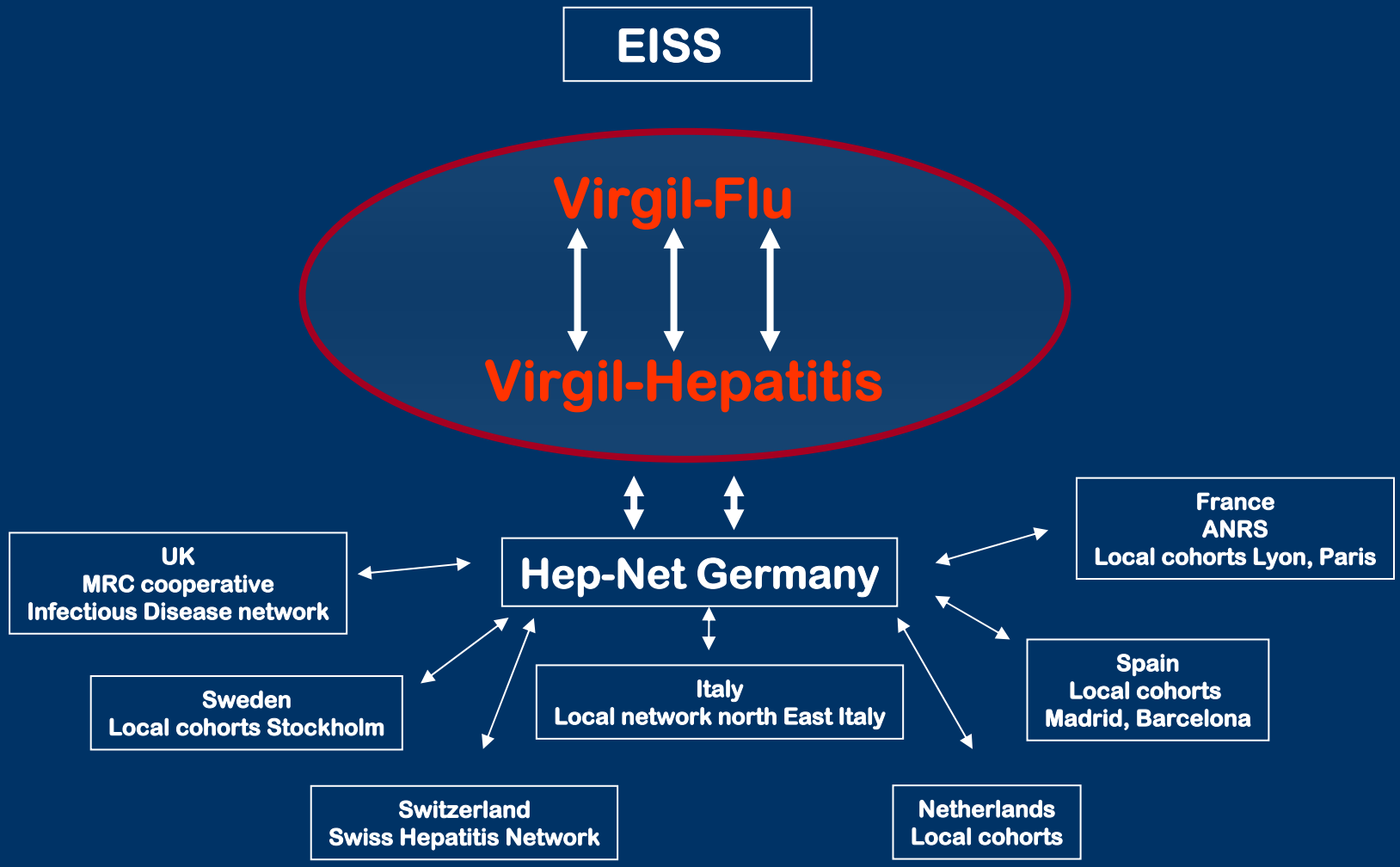
VIRGIL - Platforms

VIRGIL Surveillance Platform

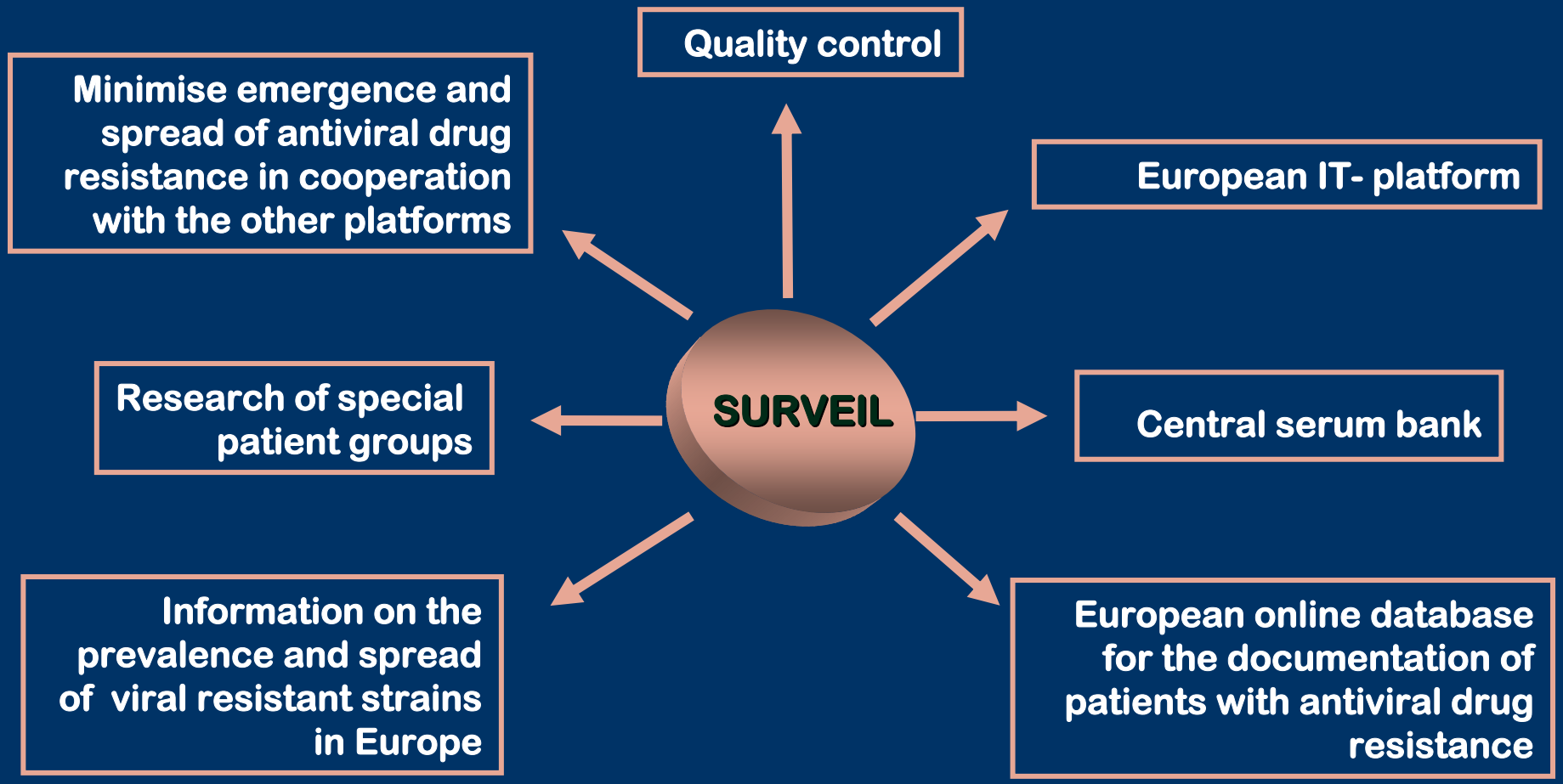
PARTNERS IN HEPATITIS SURVEILLANCE

Medizinische Hochschule Hannover (Germany) *Michael Manns*	Ludwig Maximilians Universität München (Germany) *T Mueller*	
AIES-Hospital Carlos III (Italy) *V Soriano*	Azienda Ospedaliera di Parma (Italy) *C Ferrari*	Charité Campus Virchow-Klinikum Uni Berlin (Ger) *T Berg*
Hospital Clínic Provincial de Barcelona (Spain) *X Forns*	Hospital Universitario Valle Hebron (Spain) *R Esteban Mur / M Buti*	Imperial College of Science (UK) *H Thomas*
Inserm (France) *C Trepo / F Zoulim C Brechot*	Karolinska Institutet (Sweden) *O Weiland / M Sällberg*	University of Bari (Italy) *G Pastore / T Santantonio*
The University of Birmingham (UK) *D Mutimer*	Université Catholique de Louvain (Belgium) *E Sokal*	Université de Genève (Swizterland) *F Negro*
University of Gdansk Faculty of Biotechnology (Poland) *A Podhajska*	Université Paris XII-Val-de-Marne (France) *JM Pawlotsky*	Universität des Saarlandes (Germany) *S Zeuzem*
Papageorgious General Hospital (Greece) *G Germanidis*	Tripep AB (Sweden) *A Vahlne*	Venetian Institute of Molecular Medicine (Italy) *A Alberti*

Integration of local existing networks



Main Aims of the SURVEILLANCE Network



VIRGIL - Online Database

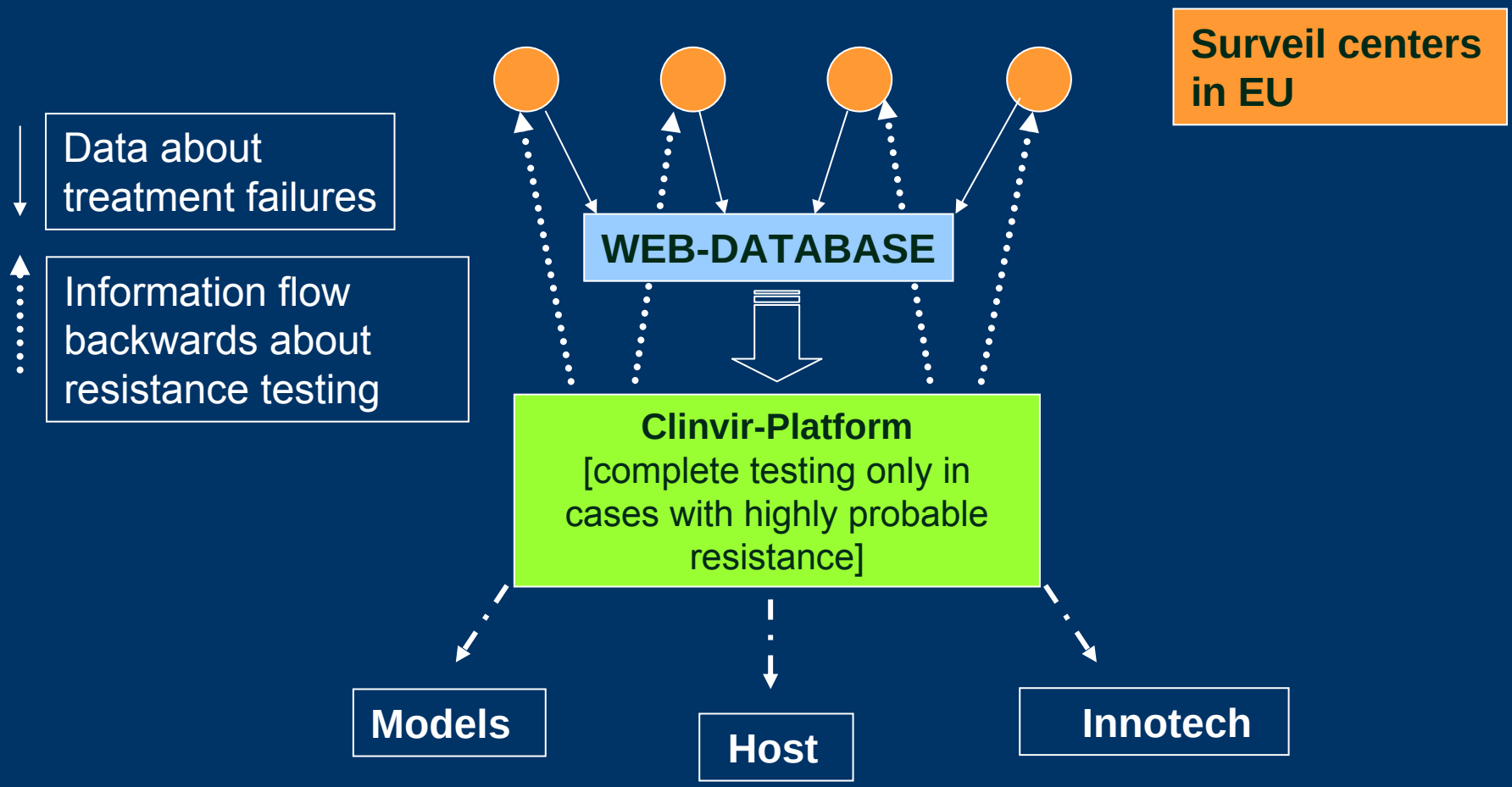
European database

1. Central Database for Europe and comprehensive IT- platform

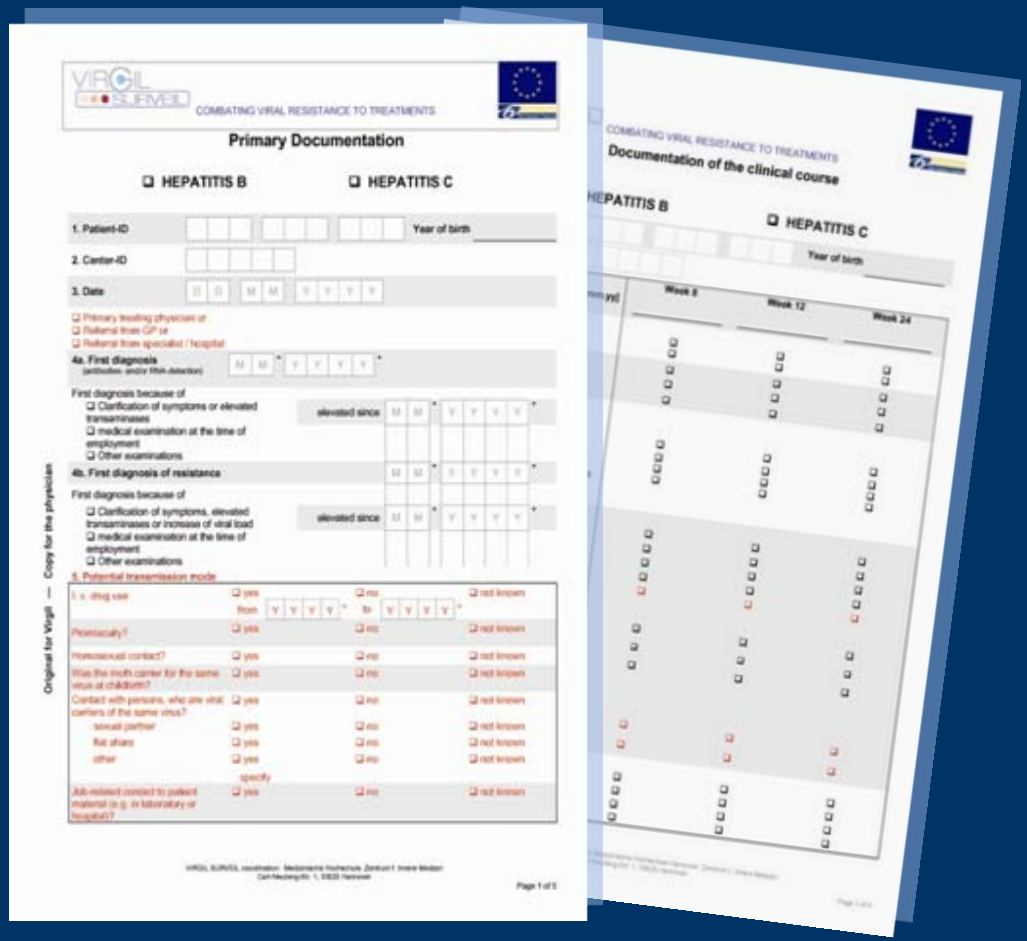
2. Serum samples

Basis for other projects, e.g. investigation of viral and host mechanisms of drug resistance

VIRGIL - Online Database

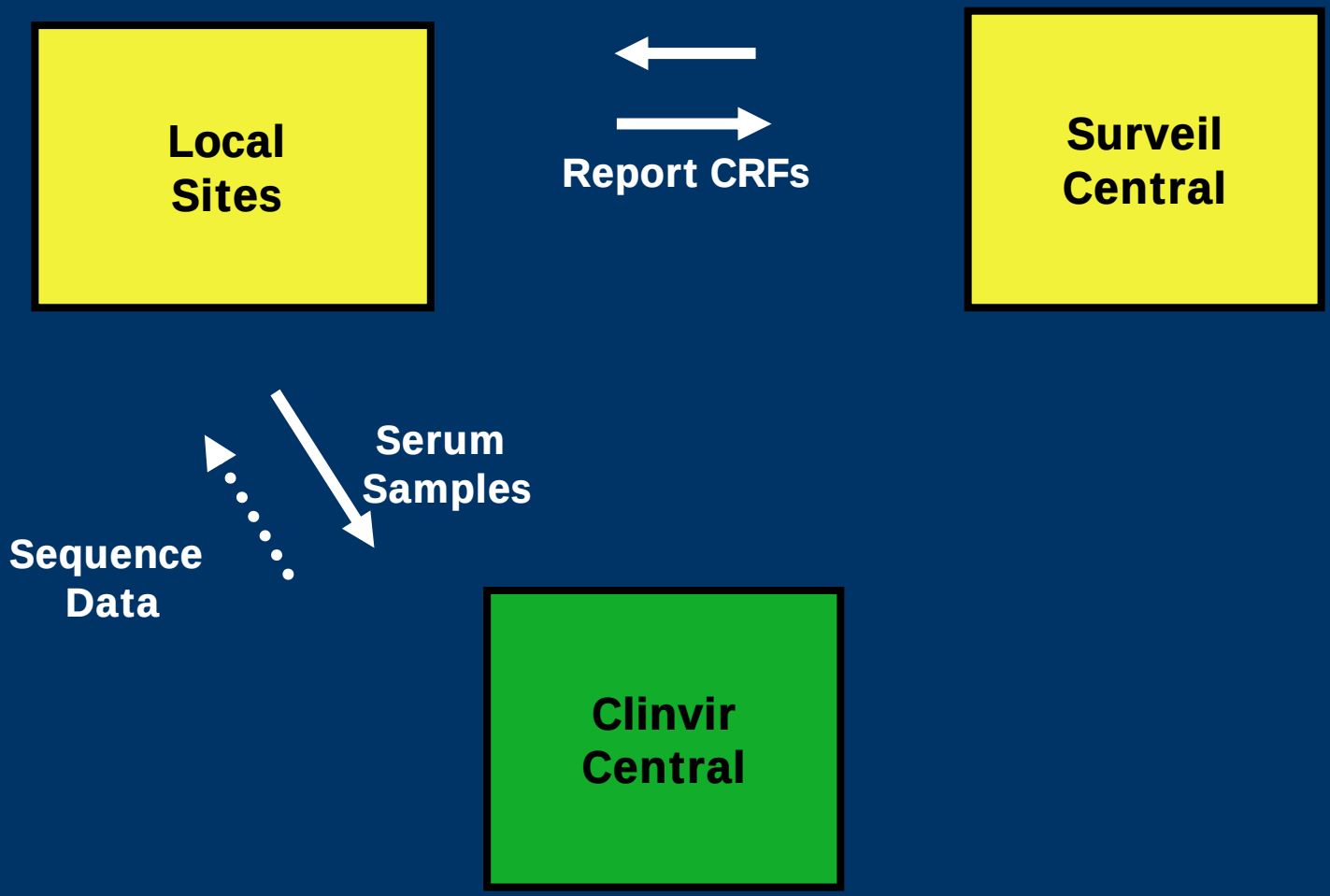


Case report forms – online documentation



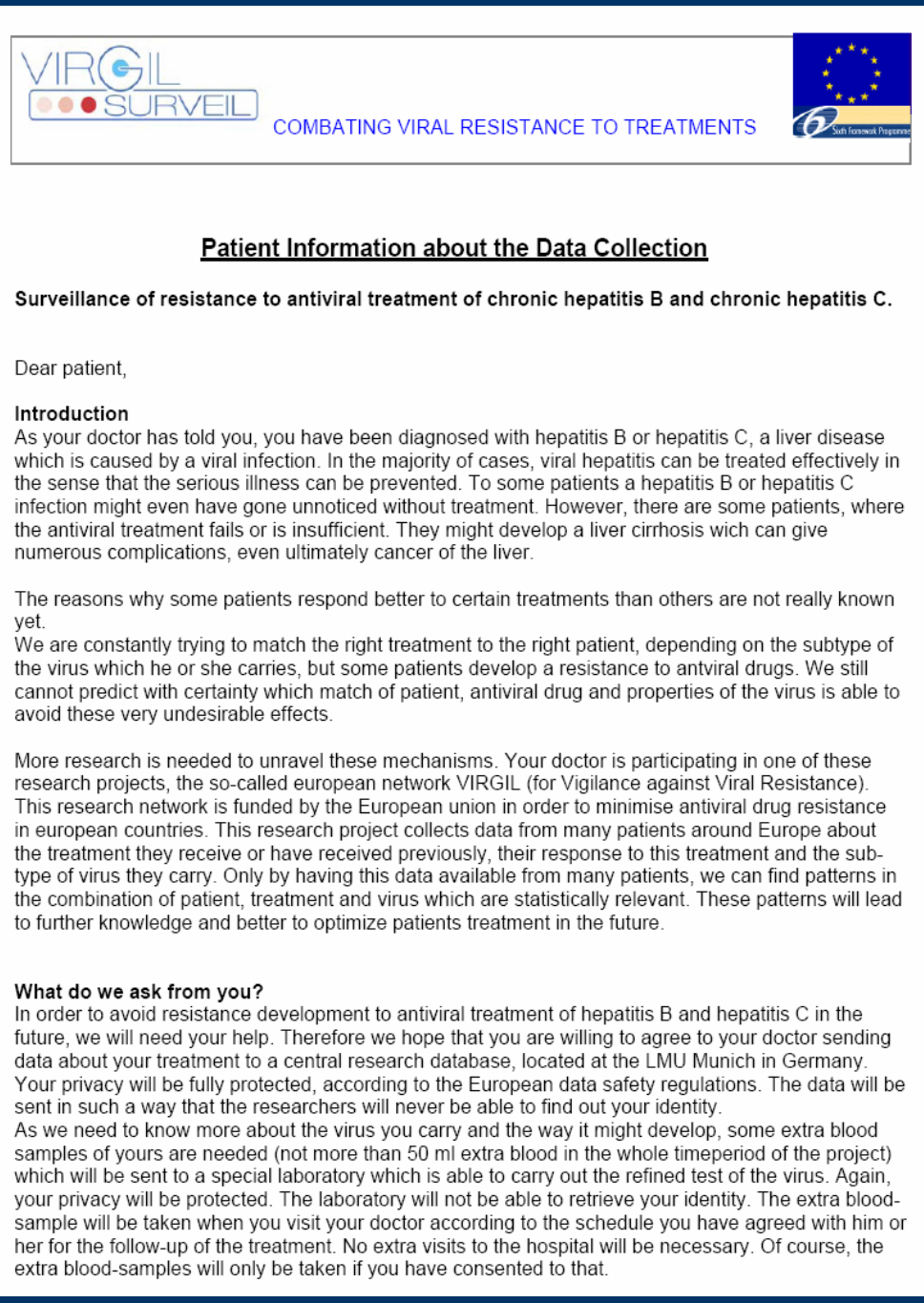
1. **Standard documentation**
2. **Primary documentation**
3. **Documentation of the clinical course**
4. **End of documentation**

Cooperation Surveil /Clinvir
- interim solution -



Patient informed consent form - available in 9 different languages

- English
- German
- French
- Italian
- Spanish
- Dutch
- Swedish
- Greek
- Türkish
- Polish
- Russian



VIRGIL SURVEIL

COMBATING VIRAL RESISTANCE TO TREATMENTS

Sixth Framework Programme

Patient Information about the Data Collection

Surveillance of resistance to antiviral treatment of chronic hepatitis B and chronic hepatitis C.

Dear patient,

Introduction

As your doctor has told you, you have been diagnosed with hepatitis B or hepatitis C, a liver disease which is caused by a viral infection. In the majority of cases, viral hepatitis can be treated effectively in the sense that the serious illness can be prevented. To some patients a hepatitis B or hepatitis C infection might even have gone unnoticed without treatment. However, there are some patients, where the antiviral treatment fails or is insufficient. They might develop a liver cirrhosis wich can give numerous complications, even ultimately cancer of the liver.

The reasons why some patients respond better to certain treatments than others are not really known yet.
We are constantly trying to match the right treatment to the right patient, depending on the subtype of the virus which he or she carries, but some patients develop a resistance to antviral drugs. We still cannot predict with certainty which match of patient, antiviral drug and properties of the virus is able to avoid these very undesirable effects.

More research is needed to unravel these mechanisms. Your doctor is participating in one of these research projects, the so-called european network VIRGIL (for Vigilance against Viral Resistance). This research network is funded by the European union in order to minimise antiviral drug resistance in european countries. This research project collects data from many patients around Europe about the treatment they receive or have received previously, their response to this treatment and the sub-type of virus they carry. Only by having this data available from many patients, we can find patterns in the combination of patient, treatment and virus which are statistically relevant. These patterns will lead to further knowledge and better to optimize patients treatment in the future.

What do we ask from you?

In order to avoid resistance development to antiviral treatment of hepatitis B and hepatitis C in the future, we will need your help. Therefore we hope that you are willing to agree to your doctor sending data about your treatment to a central research database, located at the LMU Munich in Germany. Your privacy will be fully protected, according to the European data safety regulations. The data will be sent in such a way that the researchers will never be able to find out your identity.
As we need to know more about the virus you carry and the way it might develop, some extra blood samples of yours are needed (not more than 50 ml extra blood in the whole timeperiod of the project) which will be sent to a special laboratory which is able to carry out the refined test of the virus. Again, your privacy will be protected. The laboratory will not be able to retrieve your identity. The extra blood-sample will be taken when you visit your doctor according to the schedule you have agreed with him or her for the follow-up of the treatment. No extra visits to the hospital will be necessary. Of course, the extra blood-samples will only be taken if you have consented to that.

Consent Form

Surname.....

Maiden name (if applicable) .....

Christian name(s) .....

Date of birth.....

Local patient ID .....

Address .....

Town.....

Postcode .....

I have read and understood the information about the VIRGIL project and have had time to consider my participation. If I had any questions they have been sufficiently answered.

- I agree that an extra blood sample will be taken when I visit my doctor (not more than 50 ml in the whole timeperiod of the project). These samples will be used to analyse pseudonymously the virus which I carry and its development, in a specialised laboratory. The outcome of these analyses will be linked to the data about the treatment I receive and the way I react to this treatment, however, in such a way that nobody doing such research will be able to know my identity.
- I therefore do not object that anonymous data will be sent to the research database and stored electronically in order to make this kind of research into patterns of treatment, response to treatment and the properties of the virus possible.
- I am aware that in general this research will result in better treatment options for all patients in the future and that whether I participate or not, will not directly influence my treatment or my relationship with my treating doctor. However, when I participate there is a way that in exceptional circumstances that my doctor can link my identity to the tests done in the laboratory so that my treatment can be better adapted to the sub-type of virus I carry.
- I know that I always can withdraw my consent without any steatment of reasons and this will not affect my treatment or my relationship with my doctor.
- I agree with publication of the results of this project in anonymous form.

Having read the above I voluntarily agree to participate in the VIRGIL project as described.

Date and place ..... Signature of the patient .....

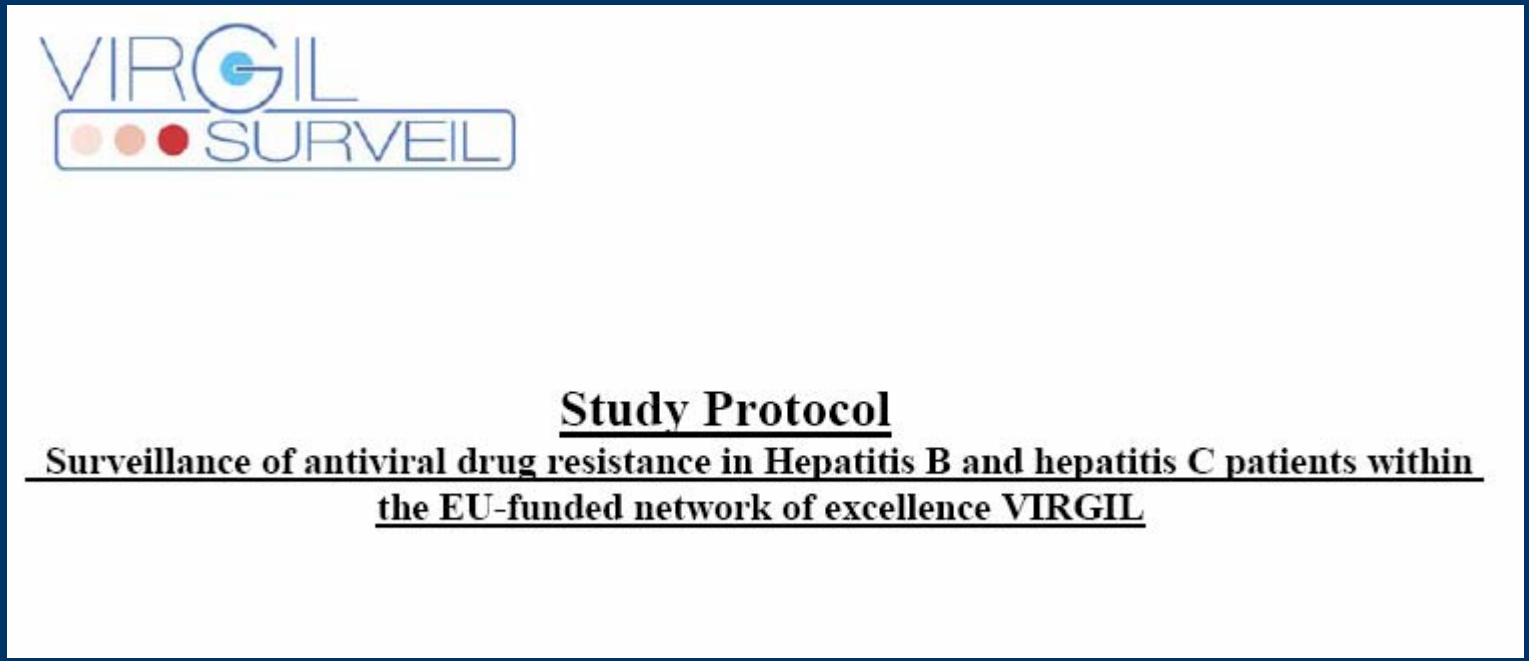
Name of the doctor.....

Date and place..... Signature of the doctor.....

VIRGIL - Online Database

19.06.2006

Positive Votum from the ethics committee Hannover



VIRGIL - Online Database

The following documents were sent to all Virgil

Surveillance partners and all additional clinicans within the Virgil Network

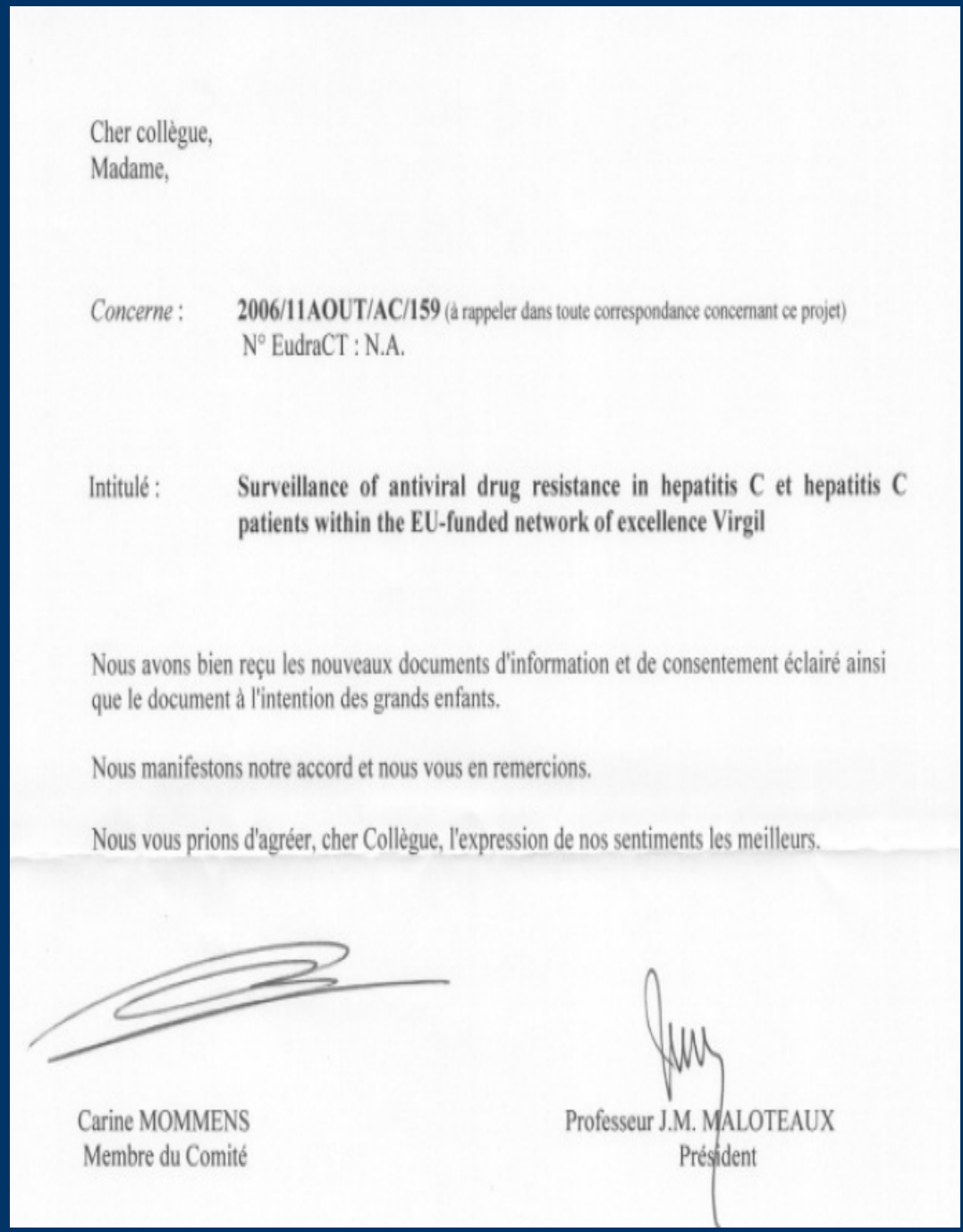
- Study protocoll
- Patient informed consent forms
- Positive votum from the ethics committee Hannover
- Case report forms

→ all partners were ask to get in contact with their own ethics committee

Problems in different countries:

- **Insurance**
- **Different patient groups**

  e.g. children



Cher collègue,
Madame,

Concerne : **2006/11AOUT/AC/159** (à rappeler dans toute correspondance concernant ce projet)
N° EudraCT : N.A.

Intitulé : **Surveillance of antiviral drug resistance in hepatitis C et hepatitis C patients within the EU-funded network of excellence Virgil**

Nous avons bien reçu les nouveaux documents d'information et de consentement éclairé ainsi que le document à l'intention des grands enfants.

Nous manifestons notre accord et nous vous en remercions.

Nous vous prions d'agréer, cher Collègue, l'expression de nos sentiments les meilleurs.

Carine MOMMENS
Membre du Comité

Professeur J.M. MALOTEAUX
Président

Virgil online database:
Two ways of documentation

1. Patients who have signed the informed consent form before or at the date of data entry should be entered as **“pseudonymised/ identifiable”** patients
   (documentation with patient initials)

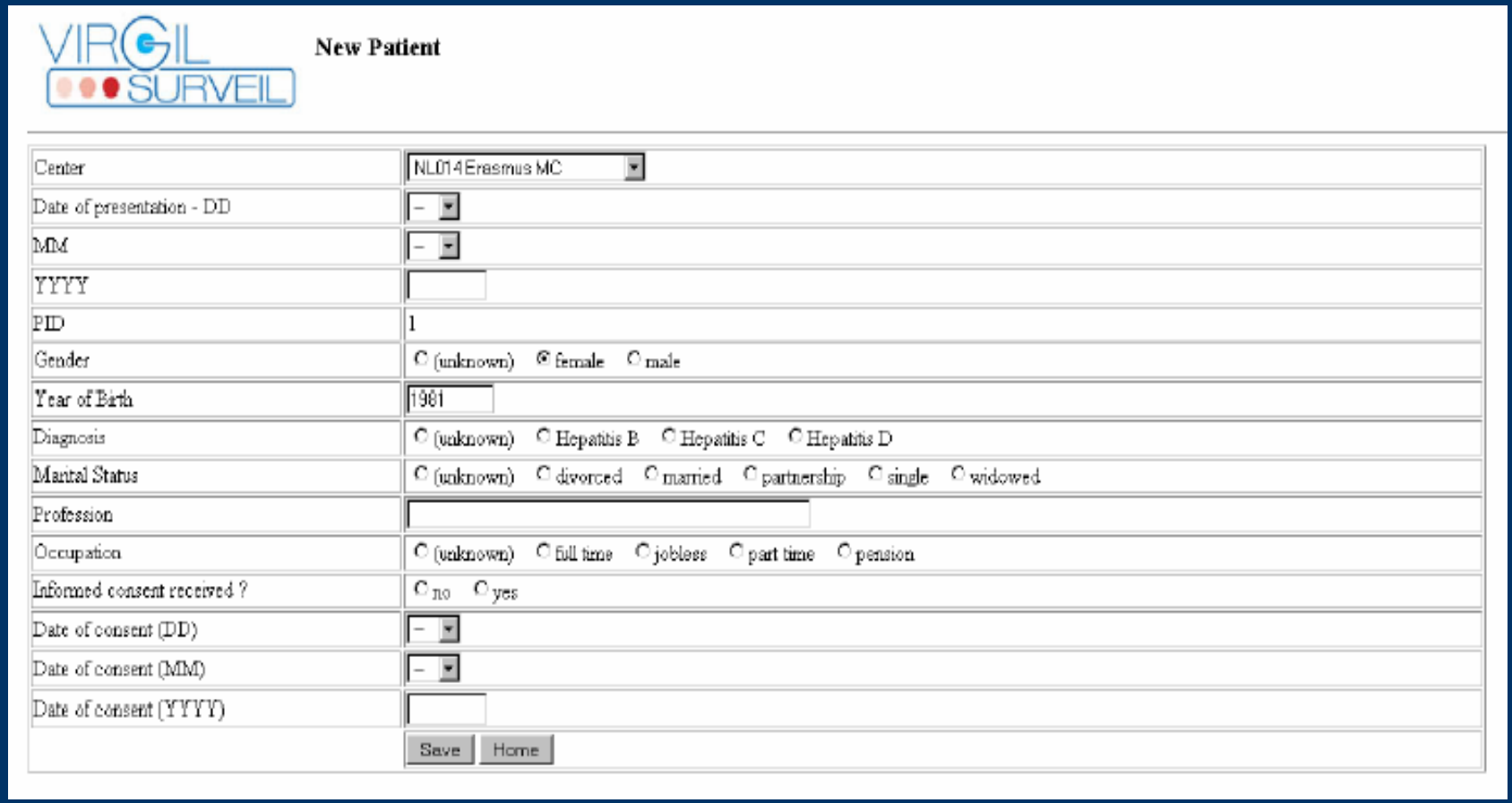
2. Patients who have not signed the informed consent form before or at the date of data entry should be entered as **“anonymised”** patients.
   (documentation without patient initials)

VIRGIL - Online Database

- Every Hepatitis B (D) and Hepatitis C patient with ongoing or previous antiviral treatment should be entered in the Virgil online database
- Every Virgil partner will receive a user name and a password to link via internet to the database
- It must be documented at each center wich patient belongs to which patient number !!!

VIRGIL - Online Database

1. Standard Documentation



VIRGIL SURVEIL

New Patient

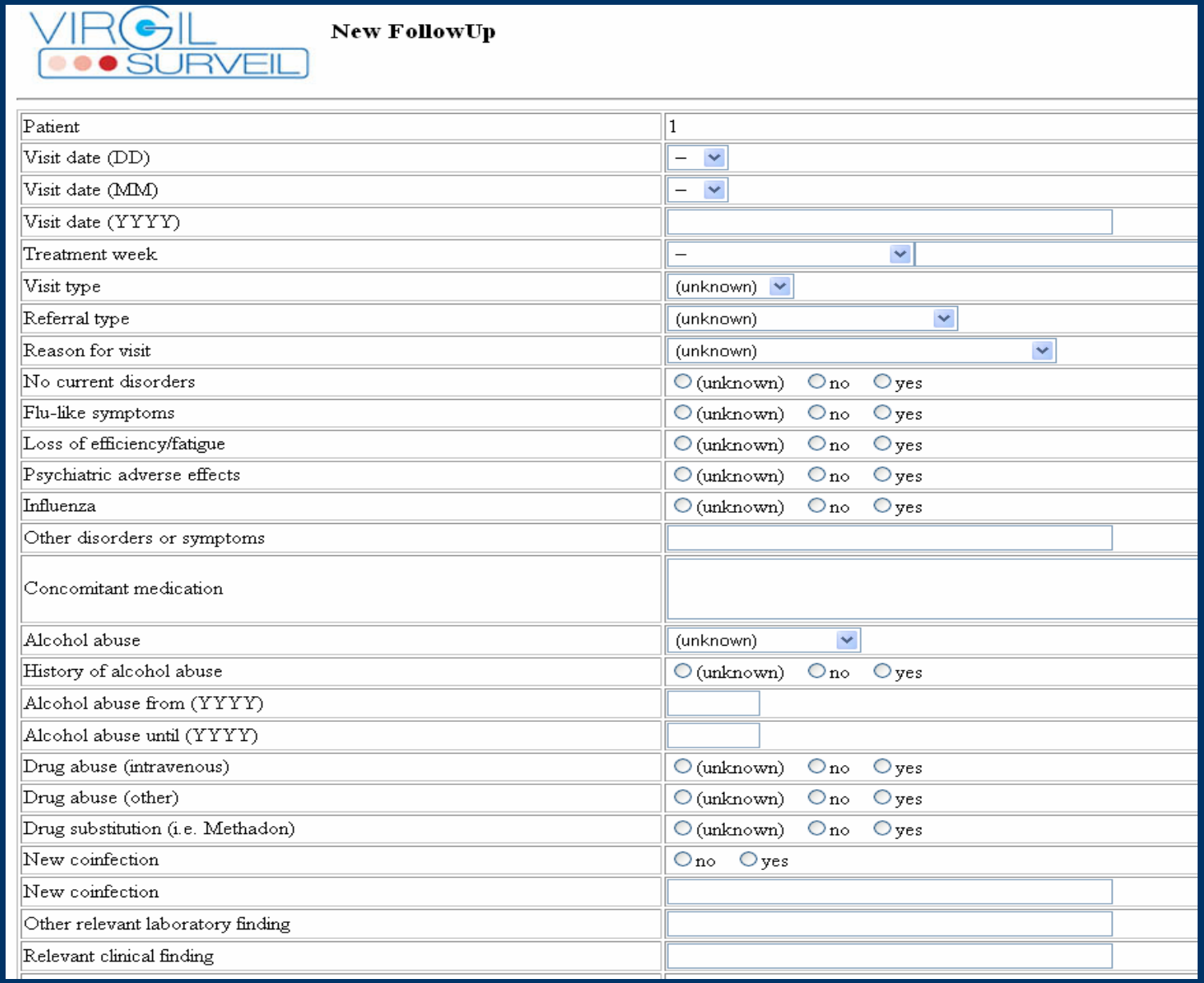
Center	NL014 Erasmus MC
Date of presentation - DD	–
MM	–
YYYY	
PID	1
Gender	○ (unknown) ◉ female ○ male
Year of Birth	1981
Diagnosis	○ (unknown) ○ Hepatitis B ○ Hepatitis C ○ Hepatitis D
Marital Status	○ (unknown) ○ divorced ○ married ○ partnership ○ single ○ widowed
Profession	
Occupation	○ (unknown) ○ full time ○ jobless ○ part time ○ pension
Informed consent received ?	○ no ○ yes
Date of consent (DD)	–
Date of consent (MM)	–
Date of consent (YYYY)	
	Save Home

2. Primary Documentation

Primary Documentation

Patient	1
Visit date (DD)	–
Visit date (MM)	–
Visit date (YYYY)	
Referral type	(unknown)
Initial diagnosis of hepatitis (MM)	–
Initial diagnosis of hepatitis (YYYY)	
Aminotransferases elevated since (MM)	–
Aminotransferases elevated since (YYYY)	
Initial diagnosis of resistance (MM)	–
Initial diagnosis of resistance (YYYY)	
Viral load elevated since (MM)	–
Viral load elevated since (YYYY)	
Drug abuse	○ (unknown) ○ no ○ yes
Drug abuse from (YYYY)	
Drug abuse to (YYYY)	
Promiscuity ?	○ (unknown) ○ no ○ yes
Homosexual contact ?	○ (unknown) ○ no ○ yes
Was the mother carrier of the same virus childbirth ?	○ (unknown) ○ no ○ yes
Is sexual partner carrier of the same virus ?	○ (unknown) ○ no ○ yes
Accommodation shared with carrier of the same virus ?	○ (unknown) ○ no ○ yes
Contact with other carrier of the same virus ?	○ (unknown) ○ no ○ yes
OtherCarrierText	
Job-related contact to patient material ?	○ (unknown) ○ no ○ yes
Other job-related risk contacts ?	○ (unknown) ○ no ○ yes
Injury with blood-contaminated instrument ?	○ (unknown) ○ no ○ yes
Surgery or other operational intervention ?	○ (unknown) ○ no ○ yes

3. Follow-up



New FollowUp

Patient	1
Visit date (DD)	–
Visit date (MM)	–
Visit date (YYYY)	
Treatment week	–
Visit type	(unknown)
Referral type	(unknown)
Reason for visit	(unknown)
No current disorders	(unknown) no yes
Flu-like symptoms	(unknown) no yes
Loss of efficiency/fatigue	(unknown) no yes
Psychiatric adverse effects	(unknown) no yes
Influenza	(unknown) no yes
Other disorders or symptoms	
Concomitant medication	
Alcohol abuse	(unknown)
History of alcohol abuse	(unknown) no yes
Alcohol abuse from (YYYY)	
Alcohol abuse until (YYYY)	
Drug abuse (intravenous)	(unknown) no yes
Drug abuse (other)	(unknown) no yes
Drug substitution (i.e. Methadon)	(unknown) no yes
New coinfection	no yes
New coinfection	
Other relevant laboratory finding	
Relevant clinical finding	

Serum samples

Every serum sample should be registered in the database before shipment

- Enter the clinical data
- Click on: SERUM SAMPLES WILL BE SEND

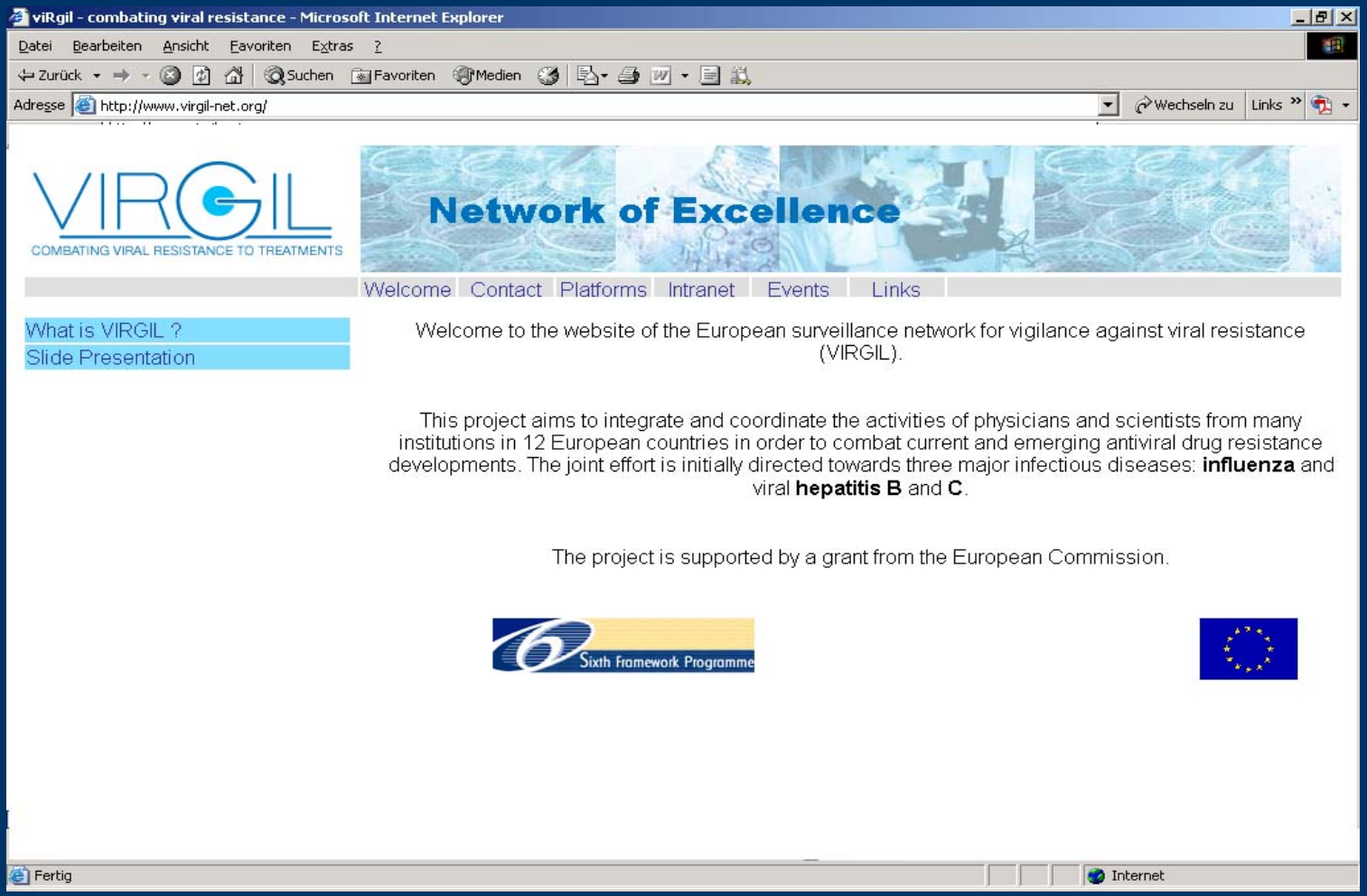
- You will receive a sample-ID, wich should be written on the tube before shipment

Proben-ID	P#ML6VZ86SL

The link between patient-ID (clinical data) and serum-ID (analysis) is only possible for the IT-Platform (Thomas Müller)

Summary

- Different legal issues in the european countries, especially for the shipment of serum samples
- Different patient groups, e.g. children
- Different regulations concering the patient insurance
- Differentiation between anonymised and pseudonymised documentation
- In some european countries is one central ethics votum not sufficient



WWW.virgil-net.org