

European orientation towards
the Better Management of

Hepatitis B

in Europe

**Recommendations of the
Hepatitis B expert group**

chaired by Dr. T. Ulmer,
Member of the European Parliament



Hepatitis B expert group:

Chair:

Dr. Thomas Ulmer MEP, European Parliament

Experts:

Prof. Michael Manns, Director Dept. of Hepatology, University of Hanover

Prof. Angelos Hatzakis, Hellenic Centre for Infectious Diseases Control

Prof. Stephanos Hadziyannis, Athens University School of Medicine and Henry Dunant Hospital of Athens

Prof. Howard Thomas, Imperial College, London

Prof. Dr. Solko Schalm, Liverdoc, Erasmus University Rotterdam

Prof. Andrzej Horban, Director Infectious Diseases Hospital, Warsaw

Prof. Nurdan Tözün, Marmara University and Turkish Association for the Study of the Liver

Prof. Pierre Van Damme, University of Antwerp

Dr. Liliana Preotescu, Institute of Infectious Diseases, Bucharest

Prof. Jean-Michel Pawlotsky, Director, French National Reference Center for Viral Hepatitis B, C and delta

Charles Gore, ELPA and Hepatitis C Trust UK

Nadine Piorkowski, President ELPA

Dr. Alex Vorsters, University of Antwerp, Viral Hepatitis Prevention Board

Penny Webb, Hepatitis B Foundation UK, Coordinator

Rapporteur and report writer:

Dr. Suzanne Wait, International Longevity Centre-UK (ILC-UK)

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Foreword

Bundesministerium
für Gesundheit

Ulla Schmidt
Bundesministerin
Mitglied des Deutschen Bundestages

Hepatitis B is frequently an inconspicuous disease. Slowly but inexorably, the chronic form destroys the liver and can even lead to cancer of the liver. In Europe alone, 14 million people are affected by the chronic form of hepatitis B. Owing to its insidious onset, those infected are frequently unaware of their condition and can therefore unintentionally infect others. The risk of transmission is ten times greater than with HIV. While chronic hepatitis B infections can only be cured in rare instances, vaccination ensures reliable protection from this disease.

I therefore highly welcome the fact that the Expert Group headed by Dr. Thomas Ulmer, MEP, has drafted the following recommendations for the prevention, screening, diagnosis and management of hepatitis B in Europe. They constitute an important element in the joint European endeavours undertaken in the fight against infectious diseases.

Published during Germany's EU Presidency, the ECDC's annual epidemiological report revealed that the number of hepatitis B cases in Europe has been decreasing overall throughout Europe during the last decade. However, this trend cannot be observed in all countries and risk groups. Consequently, further efforts are needed to stem this infectious disease wherever it has a major potential to spread.

The consistent vaccination of all newborns, children, young people and adults in certain risk groups as well as fact-based information of the population regarding the risks of hepatitis B infection and the possibilities of protecting oneself, must become a focus of European and national health policy.

The Expert Group's recommendations provide a good basis for the further development of health policy within the national responsibility of the individual Member States.

Ulla Schmidt

Preface

By: Dr. Thomas Ulmer MEP, European Parliament

In April 2006, I launched a *Call for Action* in the European Parliament to make hepatitis B a priority area for European policy. This initiative received support from MEPs from the four largest political groups and from at least 12 Member States. It drew upon discussions held at a Stakeholder Forum at the European Parliament where experts from across Europe raised the critical issues surrounding the management of hepatitis B¹.

Guidelines on different facets of hepatitis B exist and are gaining more recognition (see *Resources* below). In addition to the *Call for Action* and the Stakeholder Forum mentioned above, a number of promising initiatives aimed at raising awareness of hepatitis B have occurred over the past 2 years. These include:

- Presentation on *Threats of Hepatitis B* by Prof. Hatzakis to the management board of the European Centre for Disease Prevention and Control (ECDC) in Athens (June 2006), to encourage the ECDC to make hepatitis B a priority area for research
- A Hepatitis B stakeholders Forum in Turkey in September 2006
- A workshop on *The acute issue of chronic Hepatitis B* at the Clingendael Institute, in the Netherlands, in February 2007
- A workshop on Policies to tackle the battle against Hepatitis, in the French Senate in March 2007

As a politician and a practicing general practitioner, it has struck me that, unlike other infectious diseases like HIV/AIDS or hepatitis C, hepatitis B has not received appropriate political focus in European policy.

Why is hepatitis B important?

- *Hepatitis B is a significant problem of public health.* Every year, over 1 million Europeans are newly infected with the hepatitis B virus and 14 million people live with chronic disease within the wider Europe Region². Up to 36,000 deaths are attributable to HBV every year in Europe
- *Hepatitis B is the most common carcinogen after tobacco.* It is the cause of 80% of all cases of liver cancer worldwide
- *Hepatitis B affects twice as many people as hepatitis C*
- It is 100 times more infectious than HIV
- There are 8-10 times more people in the world living with chronic HBV than with HIV/AIDS
- *The economic burden posed by Hepatitis B on society is significant*
- *Hepatitis B is a vaccine-preventable disease.* The WHO has recommended universal hepatitis B vaccination of all newborns, children and/or adolescents against hepatitis B as well as vaccination of risk groups since 1991. Countries that have implemented widespread vaccination have seen the incidence of HBV decrease significantly among children and adolescents
- *The epidemiology of hepatitis B in Europe is changing,* with migration causing significant increases in prevalence rates. HBV does not respect geographic borders, therefore a common approach for Europe and beyond is appropriate.

1. The publication emerging from this Forum, *Hepatitis B: revealing a silent killer* is available on http://www.ilcuk.org.uk/files/pdf_pdf_21.pdf.
2. Please note that all statistics for the European Union pertain to EU-25 as European summary data for the EU-27 are not yet available.

- *There is a paucity of reliable epidemiological data on hepatitis B.* European-wide surveillance of hepatitis B is urgently needed to gain a better understanding of its changing epidemiology and identify the most effective ways to contain the disease.
- *Treatment options exist that may improve patient outcomes,* yet access to these treatments is restricted in many European countries.
- *Awareness and understanding of hepatitis B is low amongst health professionals,* as symptoms remain 'silent' for many years.
- *Uptake of vaccination, screening and treatment options remains low in at risk groups for hepatitis B.*

I should note that important strides have been made in past years to raise awareness of hepatitis B. For example, the European Association for the Study of the Liver (EASL) is updating detailed treatment guidelines which will be available in early 2008. The Viral Hepatitis Prevention Board, a scientific expert group with a focus on Europe, has been issuing and reviewing guidelines in general and hepatitis B in particular for more than 15 years.

Yet the challenge remains for an orientation towards a European hepatitis B policy. In line with the 'Health in all policies' principle, European recommendations need to look at the impact of hepatitis B on all areas of policy and try to involve all relevant European and national institutions in proposed solutions. They also need to look at the entire pathway of the disease from prevention to screening, diagnosis and treatment.

The current document is an attempt to address the needs described above. It is our hope that it may serve as a blueprint for a comprehensive policy on hepatitis B throughout Europe and that its Recommendations be adopted by Member States and then be applied at a national level across the EU and beyond

I would like to acknowledge and thank the contributors to this document, who have lent their time and expertise to making it possible during an expert meeting organised on 3 July 2007 in the European Parliament. The list of participants is presented in **Appendix 1**.

We are also grateful to Bristol-Myers Squibb and the International Longevity Centre-UK for their support and assistance in facilitation and publication of the expert meeting, and to a number of individuals for contributing their thoughts to this document. They are listed in **Appendix 2**.

And finally, it is with great pleasure that I mention that this is a collaborative effort endorsed by representatives of the European Association for the Study of the Liver (EASL), the Viral Hepatitis Prevention Board (VHPB) and the European Liver Patients Association (ELPA). We all share a common objective: to ensure that hepatitis B receives the attention it deserves of policy makers across Europe and beyond.

Thomas Ulmer, MEP and MD

1. Introduction

A. What is Hepatitis B?

The hepatitis B virus (HBV) is one of many viruses (the others being A, C, D and E) that may cause hepatitis. Hepatitis B is a viral preventable infectious disease that can lead to cirrhosis (liver damage) and liver cancer.

Five percent of the world's population is chronically infected with the hepatitis B virus – twice as many as with hepatitis C and 7 times more than with HIV. The epidemiology of the disease varies significantly from one region to another and is affected greatly by immigration. In Europe, there are 1 million new infections per year due to HBV, and 14 million people are infected with chronic disease within the wider Europe Region. Between 24,000 and 36,000 deaths are attributable to hepatitis B every year.

The natural history of hepatitis B is complex, in that it starts off as an acute disease that may then develop into a chronic condition (see Figure 1).

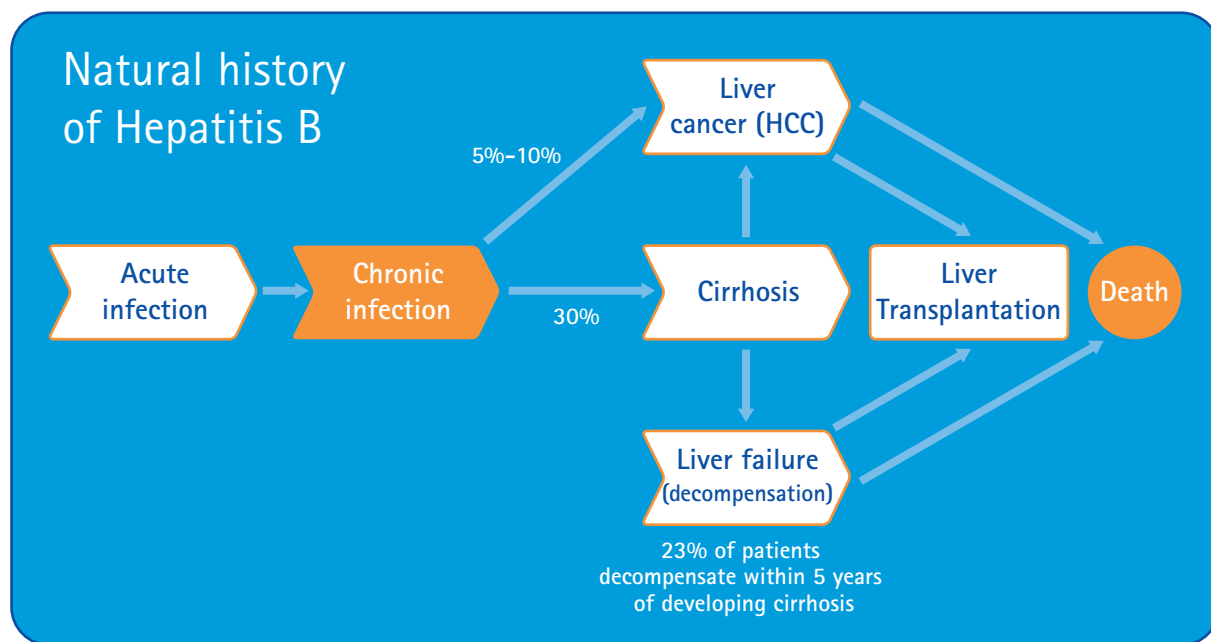


Figure 1 - Adapted from Torresi et al, 2000 and Fattovich et al, 2003³.

The risk of developing chronic disease depends on the age at which one becomes infected. Among adults, 1-5% of those infected will not be able to get rid of the virus and will develop chronic hepatitis B, and up to 1% are exposed to fulminant hepatitis. By contrast, up to 95% of those infected as newborns and 10-30% of those infected before the age of 10 years will develop chronic disease. Moreover, one person in 20 infected by HBV becomes a carrier of the virus and may infect others without incurring any symptoms themselves.

If left untreated, chronic hepatitis B evolves into cirrhosis in 30% of patients and nearly half of these will die from liver failure or liver cancer. Hepatitis B is the most common cause of liver cancer worldwide and as such is the most common carcinogen after tobacco. Liver cancer is the fifth most common cancer in man.

3. Fattovich G. Natural history of hepatitis B. J Hepatol. 2003;39 Suppl 1:S50-8; Torresi J, Locarnini S. Antiviral chemotherapy for the treatment of hepatitis B virus infections. Gastroenterology. 2000 Feb;118 (2 Suppl 1):S83-103. Review.

Burden of illness

The economic cost associated with hepatitis B is considerable and costs escalate with the increasing severity of illness (Brooks et al., 2001). Costs include direct costs of treatment for hepatitis B as well as indirect costs linked to lost productivity and premature death of those affected. Studies on the direct medical costs for the management of different stages of chronic hepatitis B disease in France, Italy, Spain, UK (Brown et al., 2004), Germany (Dale et al., 2006), and Sweden (De Cock et al., 2006) showed a non-linear increase in average annual costs as the disease progressed from the early stages to later stages such as decompensated cirrhosis and liver cancer. For example, in Germany, the annual cost of chronic hepatitis B management increases from approximately €3000 per patient at the stage of chronic active hepatitis, to approximately €15,000 at the liver cancer stage. In a South Korean study conducted in 1997, the authors found that direct costs of hepatitis B were the equivalent of 3.2% of national GDP and indirect costs represented over 20% of total costs (Yang et al, 2001).

Routes of infection

Hepatitis B is a viral infection that is transmitted by contact with the blood or body fluids of an infected person. The principal routes of infection are blood-borne and sexual. The virus is 100 times more infectious than HIV and 10 times more infectious than hepatitis C, thus the risk of infection upon exposure is very high.

The main groups at risk for contracting hepatitis B are:

Table 1. Persons at risk for Hepatitis B

- Men who have sex with men
- Heterosexual persons with multiple sex partners
- Injecting drug users who share or have shared needles
- Persons with a history of sexually transmitted infection (STI)
- Household contacts of those infected with HBV
- Newborns of HBV-infected mothers
- Sex partners of those infected with HBV
- Inmates of long-term correctional facilities and prisons
- Patients undergoing hemodialysis
- Healthcare workers and public safety workers with frequent blood contact
- Clients and staff at institutions for the developmentally disabled
- Recipients of certain blood products and transfusions
- Travelers to areas of high HBV endemicity

Source: CDC 2004

Management of Hepatitis B

Management of hepatitis B consists of prevention, including vaccination, screening, detection and diagnosis, and treatment.

Vaccination against hepatitis B has been shown to be 95% effective at preventing acute and chronic HBV and countries that have implemented widespread vaccination have seen incidence of HBV decrease significantly among children and adolescents. The WHO has recommended universal hepatitis B vaccination of all children and adolescents against hepatitis B as well as vaccination of risk groups since 1991. Vaccination policies differ across Europe, however, with countries such as the UK, the Netherlands and Nordic countries having opted not to include hepatitis B in their routine vaccination schedules.

It is important to note that vaccination cannot prevent chronic hepatitis from occurring in those already infected.

Hepatitis B is a silent disease in that symptoms are difficult to identify and may even be absent in up to 40% of cases. As a result, infected individuals may ignore that they are infected for years and health professionals often fail to diagnose the disease in its early stages. The absence and difficulty of identifying clear symptoms in acute hepatitis B makes screening of people at risk critical and diagnosis extremely important (Wong and Pomfret, 2007).

Indeed, *screening* of high-risk individuals for hepatitis B is essential for early identification and treatment of those infected. Screening allows to guide individuals infected with HBV to appropriate care and help them prevent the infection of others. It also allows for household and sexual contacts of infected individuals to be offered vaccination (Valla et al, 2003).

Diagnosis of hepatitis B at an early stage may be critical in halting the progression of disease and limiting the risk of infection by affected individuals.

Treatment consists mostly of antiviral therapy and supportive therapy. Effective antiviral therapies have been shown to slow the progression of disease in those with chronic hepatitis B and delay the onset of cirrhosis (Liaw et al, 2004). For patients who develop end-stage cirrhosis, the only possible treatment is liver transplantation

B. The current document

The purpose of this document is to present key Recommendations that may help build a cohesive European policy on the management of hepatitis B. It is not a clinical guideline, nor does it attempt to cover all aspects of hepatitis B in depth. It is a *policy document* and aims to raise awareness amongst European as well as national policymakers of the critical importance of hepatitis B in Europe and beyond and encourage all stakeholders to take ownership for the better management of hepatitis B within their respective spheres of activity.

To this end, the Recommendations propose critical areas where policies are needed and offer a practical list of actions that, if implemented, may help pave the way to improving the prevention and management of Hepatitis B across Europe and beyond. A full list of references and resources on hepatitis B is provided at the end of this document.

2. Recommendations: towards the better management of Hepatitis B

A. Awareness and Prevention

A¹. European leadership

- The "Call for Action" on Hepatitis B, this Orientation document as well as the Written Declaration on Hepatitis C should be seen as complementary documents for a comprehensive EU policy on viral Hepatitis
- The European institutions should encourage national policy-makers to work towards the implementation of the policy recommendations set out in these documents
- The European Commission should set *clear public health objectives* that may be quantified at each country level for the gradual eradication of hepatitis B⁴
- Hepatitis B should be a focal point of Hepatitis Awareness Day 2008

Europe must take the lead in recognising chronic hepatitis B as one of the most important blood-borne and sexually transmitted infections and make it a priority area for public health policies and action.

The European Commission should involve hepatitis B advocacy groups and professional and scientific societies in developing a holistic strategy to improve the prevention, control and clinical management of hepatitis B across Europe.

A². A holistic European strategy

- This comprehensive European strategy should aim to improve the prevention and management of hepatitis B and the *quality of life* of those affected by the hepatitis B virus (HBV) in all European countries
- This document should follow the '*Health in all policies*' principle and examine the implications of hepatitis B within all relevant areas of policy⁵
- National governments should follow the lead of the Commission and *transpose this European strategy to reflect their national legislative framework* and policy areas
- Patient groups and European professional and scientific societies must be involved as key partners in policy development at EU and national levels

4. Two interesting examples are the Health for All 2010 public health targets set in the United States, which specify quantifiable goals for the reduction of hepatitis B cases in specific risk groups and the French 'Loi relative a la sante publique' established in 2004, which mentions the reduction of hepatitis cases (in general) by 30% by 2008 as one of its core goals.

5. Areas of policy that require particular attention include: health, social care, immigration, education, adoption, health and safety at work, public health, anti-discrimination legislation, privacy and data protection.

A³. Social integration of individuals infected with HBV

- National strategies to improve the management of hepatitis B must recognise that, like HIV/AIDS, hepatitis B is a chronic condition that may lead to the *stigmatisation of those affected*
- All strategies should thus include: the *protection of the rights* of individuals infected with HBV, support services for them and their families, and awareness building programmes to improve the understanding of hepatitis B by the general population

National policies on hepatitis B must have as an explicit goal the social integration of individuals infected with the hepatitis B virus and seek to actively protect their human rights and combat against stigma and discrimination against them.

A⁴. Clear and consistent messages to the public

- Advocacy groups should work with policymakers, public health departments, health professionals and other stakeholders to ensure that, wherever they access the health system, individuals are offered *the same, complete information* on prevention, screening and treatment options for hepatitis B
- In particular, targeted efforts are needed at the national level to *raise the standards of training offered to all health professionals* who may come into contact with individuals at risk of becoming infected with HBV or who are already infected by HBV

Clear and consistent messages related to hepatitis B must be communicated to the general public by governments, NGOs, public health officials and primary care clinicians in order to raise awareness and understanding of the disease and overturn misconceptions about Hepatitis B and to eliminate Hepatitis B and liver cancer as a serious health problem.

A⁵. A cohesive policy of universal vaccination across Europe

- Currently, vaccination practices vary considerably across Europe, with countries such as the United Kingdom, the Netherlands and Nordic countries having chosen not to include the hepatitis B vaccine in national childhood or adolescent vaccination schedules
- Given the high levels of immigration within the EU, this lack of uniformity in vaccination policies *threatens the potential for EU-wide strategies to contain the spread of HBV*. Thus a uniform policy of vaccination is needed across the EU

In line with WHO recommendations, Europe should encourage a cohesive policy of universal vaccination of all newborns and adolescents as well as effective vaccination of populations at risk

Table 2. WHO recommendations for vaccination against Hepatitis B

Infants:

- All infants should receive a full schedule of hepatitis B vaccine as part of the national vaccination recommendations
- Babies of infected mothers: All babies of pregnant women infected with HBV should receive a full course of immunisation starting from birth. Midwives and obstetricians must discuss with the mother the importance of infant vaccination and ensure that access to a full course of vaccination is given

Children:

- Infants and adolescents not vaccinated previously should receive a full course of hepatitis B vaccine (catch up vaccination)

Adults at risk:

- Adults belonging to groups at risk of infection from HBV (see Table 1) should be offered vaccination within their regular health settings

Given the disproportionate prevalence of hepatitis B among immigrants, vaccination of all individuals intending to take permanent residency in the EU should be recommended across Europe.

A⁶. Recommended vaccination to immigrants

- The incidence of hepatitis B amongst immigrants, particularly those from countries of high or intermediate HBV endemicity, is much higher than among 'national' populations in most EU countries⁶. Thus targeted vaccination is needed to *reduce incidence rates within these populations*
- Vaccination programmes for immigrants must include full follow-up for all persons vaccinated. In particular, if the response to vaccination is negative in an individual, then he or she should be screened for HBV antibodies and offered all appropriate care, counseling and treatment options as a health services package

A⁷. Integration of hepatitis B prevention into existing public health frameworks

- As childhood vaccination programmes do not impact on incidence of HBV amongst adult at risk groups, targeted efforts are needed to ensure that those individuals at risk are offered vaccination⁸
- Risk-based vaccination policies for adults must take into consideration the fact that many persons at risk will not identify themselves as 'at risk' for hepatitis B and may face particular barriers of access to care. Therefore education and information campaigns are needed
- National hepatitis B strategies should thus examine whether all opportunities are taken to integrate hepatitis B prevention messages into existing policies and programmes where populations at risk may be reached (see Table 3)

Hepatitis B prevention and control strategies must be integrated into existing public health programmes to ensure that at risk populations are reached and offered appropriate prevention, screening and treatment in accordance with their needs.⁷

6. In the UK for example, in 2006 there were 450 new cases of hepatitis B among UK nationals as compared to 4000 amongst individuals belonging to immigrant communities (Thomas H., personal communication).

7. In March 2007, the Euro Mediterranean Parliamentary Assembly (EMPA) adopted an amendment calling for better prevention, screening and treatment of pregnant women at risk of HBV in Maghreb and Mashreq countries.

8. Whilst childhood vaccination policies have demonstrated success in reducing the incidence of hepatitis B in vaccinated populations in several countries, a similar decrease amongst adult at risk groups has often not been observed.

EU Funded projects are needed to prevent the transmission of hepatitis B among injection drug users (IDUs) and prisoners.

A⁸. Programmes for prisoners and injection drug users

- Two of the most difficult to reach groups at risk of hepatitis B are prisoners and IDUs
- Prisoners are at high risk of contracting hepatitis B due to the high prevalence of homosexual activity and injected drug use whilst in prison as well as previous behavioural risks
- Injection drug users (IDUs) are at very high risk for infection through multi-person use of injection equipment and through unprotected sexual contact
- Dedicated projects targeting these two vulnerable populations must address: i. the need to reach IDUs and prisoners before they are exposed to HBV, ii. discrimination suffered by prisoners and IDUs from health care providers, iii. financial barriers to vaccination, and iv. difficulties in completing the 3-injection vaccination series
- In all programmes, IDUs and prisoners must be treated as full citizens entitled to health care of the highest standard⁹

Table 3. Needed components of integrated vaccination programmes against HBV

For *integrated vaccination programmes* to work within public health settings (STI clinics, walk-in centres, primary care clinics, HIV counselling services,...) the following are needed:

- staff education and training
- vaccine availability
- consistent funding for administration to adults
- trained personnel to administer the vaccine
- clear data systems as users will access different points of contact
- dedicated funding for at risk vaccination programs against hepatitis B within existing public health settings

Source: Hershey et al, 2005

A⁹. Protection of health care workers

- Each year in Europe, 304,000 health care workers are exposed to at least one percutaneous injury with a sharp object contaminated with HBV
- Policies and training programmes on health worker safety should recognise that the *probability of acquiring an infection after occupational exposure in the absence of vaccination or post-exposure prophylaxis is 20-40%* for HBV, which is much higher than for hepatitis C (0.5%) or HIV (<0.3%)
- Vaccination of healthcare workers is obligatory in many EU countries, however it should be more universally applied throughout the EU
- All healthcare institutions should have a system readily available to deal with any occupational exposure to hepatitis B for their personnel. These programmes should include *prevention of HBV as well as management of risk* once a health care worker has been infected (see Table 5)

The European Commission and the Council should respond to the recommendations of the June 2006 European Parliament Resolution on the protection of European workers from blood-borne infections due to needlestick injuries and make special consideration for the risks of contracting hepatitis B.

9. EU policy background: The Council recommendation of 18 June 2003 on the prevention and reduction of health-related harm associated with drug dependence recommended on paragraph 9 to 'promote adequate hepatitis B vaccination coverage and prophylactic measures against HIV, hepatitis B and C, tuberculosis and sexually transmitted diseases, as well as screening for all the aforementioned diseases among injection drug users and their immediate social networks, and take the appropriate medical actions'. This Recommendation led to a Strategy and Action Plan. A dedicated funding stream under the 2003-8 EU Public Health Programme was also created to implement sustainable 'harm reduction programmes among vulnerable groups to prevent transmission of infectious disease... among prisoners, injection drug users (IDUs) and their sexual partners and from mother to child. (DG Sanco 2007).

Table 4. Principles governing the development of HBV prevention strategies aimed at prisoners

- On entry into prison, all prisoners should be offered information on the risks of blood-borne and sexually transmitted infections, including hepatitis B
- All prisoners should be offered screening and, if indicated, free vaccination, preferably with a shorter course to increase compliance as well as screening
- Counselling and treatment options should be explained to prisoners by a knowledgeable health worker
- Preventive means such as free condom provision should also be available to prevent sexual transmission of hepatitis B and other STIs
- National ministries of health should work with the prison health services, parole and probation officers and reintegration programmes to ensure continuity of information and treatment for prisoners entering and leaving the prison system
- Special consideration for the ethnic origins of many prisoners should be taken in the provision of information materials on hepatitis B
- All prison staff should be vaccinated against hepatitis B as they run the risk of contamination through handling pockets and bags for concealed needles and weapons

Source: *European Guidelines on HIV/AIDS and hepatitis in prison (HIPP 2001)*

Table 5. Necessary components of healthcare worker protection programmes against HBV¹⁰

i) Prevention:

- All health care workers should be vaccinated against hepatitis B
- Educational programmes for all personnel on the risks of exposure
- Safe sharps disposal systems
- Personal protective equipment
- Safety-engineered sharp devices to ensure a safe working environment for all

ii) Management:

- Written protocols for prompt reporting of any incidents
- Evaluation, counselling, treatment and follow-up of any occupational exposure that may put a health care worker at risk of a blood-borne infection
- Health care workers who have positive markers to hepatitis B should be counselled regarding their need for medical evaluation and treatment
- Evaluation of the risk that HBV-infected health care workers pose to patients should be assessed by an expert review panel according to national and international recommendations

Source: *Gunson et al, 2003; European recommendations (2005), World Health Assembly (2007); VHPB Recommendations*

10. Note: These precautions should indeed extend to the prevention of blood-borne infections in general in health care settings.

B. Surveillance

B¹. European-wide surveillance

- Since 2006, the European Centre for Disease Prevention and Control has responsibility for reporting hepatitis B surveillance across Europe¹¹. Their first surveillance report, published in June 2007, found significant heterogeneity in the availability and quality of data on hepatitis B across Europe¹²
- EU funds should be dedicated to support national surveillance systems for hepatitis B to ensure that they meet *similar standards across the EU* (see Table 6). This initiative should be coordinated through the ECDC

An EU-wide surveillance network for hepatitis B needs to be developed with the collaboration of the European Centre for Disease Prevention and Control and in line with the EUROHEP.NET recommendations for surveillance of hepatitis B across Europe.

Table 6. Principles that should govern national surveillance systems on hepatitis B¹³

- Develop a mandatory surveillance system that is able to distinguish cases of acute hepatitis B from chronic hepatitis B
- Develop an easily-applicable minimal dataset to ensure uniform data collection across all surveillance centres
- Measure the burden of illness posed by hepatitis B, including hospitalisations and sequelae
- Collect data on antiviral therapies to identify resistance patterns
- Collect a registry of hepatitis deaths and link these data to surveillance
- Record cases of liver transplantation and link these data (eg. through EuroTransplant) to surveillance systems for hepatitis B
- Perform 10-yearly seroprevalence studies, particularly in certain risk groups in countries with changing epidemiology
- Build in the ability to audit systems to ensure quality data collection.

Source: EUROHEP.NET expert report

B². Mandatory notification of chronic and acute disease

- Incidence rates of hepatitis B have been decreasing across Europe due to vaccination and changes in risk behaviours. However, these figures reflect only acute cases of hepatitis B. The prevalence of chronic hepatitis B and of hepatitis B carriers is actually increasing, mostly due to migration. However, this fact is hidden due to lack of reliable data that tracks carrier rates and chronic cases of hepatitis B throughout Europe
- It is essential to develop reliable data collection systems that measure the *full burden posed by hepatitis B*, in terms of acute and chronic disease, so that appropriate public health measures may be taken to reduce this burden¹⁴

Chronic as well as acute hepatitis B should become a notifiable disease across Europe to ensure that accurate data on the burden of illness posed by hepatitis B is recorded across Europe.

11. Until 2005, a European-wide surveillance network for hepatitis B existed under the form of EUROHEP.NET. This EU project ended in 2005. The EUROHEP.NET expert report outlining their recommendations for continued surveillance of hepatitis B across Europe may be found on <http://www.eurohep.net/files/reports/Recommendationsdec2005.pdf>.

12. The First European Communicable Disease Epidemiological Report, ECDC (p. 132-137) – 7 June 2007.

13. These recommendations are based on the EUROHEP.NET expert report submitted to the European Commission in 2005. A request to set up a EU surveillance network was also made in Commission Decisions 2000/96/EC and its amendments 2003/534/EC and 2003/542/EC.

14. This was, in fact, one of the leading recommendations of the EUROHEP.NET expert report mentioned previously.

Systematic screening for hepatitis B should be available to all persons at risk within all relevant health care and community settings.

C. Screening

C¹. Screening offered in all health and community settings

- Individuals at risk of having been infected by the hepatitis B virus or at risk of being carriers of the HBV should be screened for HBV at every opportunity
- In particular, all HIV-positive persons should be tested for hepatitis B markers as they carry an increased risk of also being infected with HBV¹⁵
- Every effort should be made to offer full screening services for hepatitis B within all settings where individuals at risk may be present or may present for care (see Table 7)
- National public health authorities and health services must ensure that sufficient resources are allowed to centres offering HBV screening to ensure that appropriate follow-up information, counselling and care are available to those requesting screening
- All sero-negative persons should be offered a full course of vaccination against hepatitis B and efforts should be made to optimise compliance with the full schedule offered

C². Engagement of local community leaders to encourage screening

- Grass-roots efforts to *engage community leaders* have proven successful in raising awareness within immigrant communities of the risks of hepatitis B and encouraging individuals to take responsibility for containing the risk of infection and to seek appropriate prevention and treatment if infected¹⁶

Grass-roots outreach and communication initiatives should be funded by national governments to engage local communities with high proportions of immigrants from high-prevalence countries in the prevention of hepatitis B within their communities.

Table 7. Settings where screening for hepatitis B should be available

- Prisons
- Public health clinics
- Walk-in clinics
- Community centres
- Sexually-transmitted infections (STI) clinics
- Adolescent health clinics
- Blood transfusion centres
- HIV clinics
- Injection Drug User (IDU) support facilities
- Immigration offices
- International adoption agencies
- Hospital out-patient departments
- Emergency rooms
- Facilities encountered by people with a severe mental illness (psychiatric departments in hospitals, community centers)

15. As suggested by the European Parliament Resolution on Combating HIV/Aids within the EU and in the neighbouring countries 2006-2009 adopted on 24 April 2007 and acknowledging "the frequent dual diagnosis of HIV and hepatitis... [and urging] action to treat and care for such patients"(Paragraph 37).

16. For example, leading UK hepatologists have worked with a hepatitis advocacy group to go into mosques and temples of communities known to have a high endemicity of hepatitis B. They have engaged the resident imam or spiritual leader to speak to the congregation about hepatitis B and encourage them to seek appropriate prevention and care.

C³. Antenatal screening

- Transmission from mother to child is one of the most common modes of transmission for the HBV. Thus *all pregnant women should be screened* for HBV markers and all babies should be vaccinated at birth¹⁷
- Maternal health policies should be aware that lack of prenatal care may be particularly prevalent amongst more *vulnerable women*, immigrants, injecting drug users and women who have other barriers of access to care
- Obstetrics wards should have *trained staff available* to screen pregnant women on admission to hospital for delivery and administer the hepatitis B vaccine to newborns¹⁸
- Obstetrics wards must also have resources in place to refer women who are HBsAg positive to *appropriate case management programs* to make sure that their infants receive post-exposure seroprophylaxis, vaccination and follow up (CDC 2005)

All pregnant women should be offered antenatal screening for Hepatitis B as part of their prenatal care, as per WHO recommendations. For women who do not attend prenatal care, screening should occur when the woman enters the hospital for delivery.

Immigration and public health policies should ensure that all immigrants from countries with high or intermediate endemicity for HBV are screened for HBV within appropriate healthcare settings. All family members and household contacts of persons who test positive (HBsAg+) for HBV markers should be vaccinated.

C⁴. Screening available to all immigrants

- Screening services should be offered *in parallel with vaccination* against hepatitis B (see Recommendation A6) to all immigrants who intend to take up permanent residency within the EU
- Clear guidelines are needed within screening centres to ensure that disclosure of information about the HBV status of individuals is made in accordance with the individuals' wishes and in full respect of privacy laws.
- The human rights and civic liberties implications of screening of immigrants must be considered and addressed explicitly in all governing policies.

17. Infants infected at birth have a 90% risk of becoming chronic carriers. Immunisation has been found to prevent infants from becoming carriers in up to 95% of cases (Hadler and Margolis, 1992).

18. Midwives and GPs may play an important role in ensuring that women receive appropriate information about the risk of hepatitis B, treatment options and implications for the child (DoH 2000).

C⁵. Blood safety in donor banks

- Appropriate regulation, protocols and safeguards must be in place to ensure the safety of blood banks and blood donations, in line with the EU Blood Safety Directive (2002)
- *Better transparency and clarity* on policies for the management of donors and units that test positive for hepatitis B virus are needed across Europe, as countries follow different policies for transfusion safety depending on the levels of endemicity of hepatitis B in their populations

The blood of all potential donors must be screened for hepatitis B using the most appropriate screening techniques. Full notification of possible infection to donors must be ensured whilst protecting their anonymity.

C⁶. Screening for liver cancer

- Liver cancer screening is important because most patients have appearance of perfect health, showing no symptoms until it is already too late.
- Regular liver cancer screening involving both blood tests and ultrasound tests are essential because liver cancer can occur even in patients without cirrhosis.

Liver cancer caused by chronic Hepatitis B infection often develops between 30 to 65 years of age. Regular screening for liver cancer amongst chronically infected patients should start at the age of 30 years or younger.

D. Detection and treatment

D¹. Effective treatment exists

- Treatment of patients with chronic hepatitis B has been shown to *delay clinical progression of disease* to cirrhosis and advanced fibrosis as well as reducing the risk of hepatocellular carcinoma. (Liaw et al, 2004)
- In many ways, the fact that vaccination programmes exist may have taken the attention away from treatment options and their importance for managing the disease
- Patients diagnosed with Hepatitis B should receive treatment in line with agreed upon Clinical Practice Guidelines
- *Regular screening for liver damage* is necessary to determine when initiation of Hepatitis B treatment is appropriate
- *Access to treatment must be improved* particularly for 'difficult to reach' populations, such as immigrants or IDUs, who may face financial and other barriers to treatment

Access to treatment for hepatitis B must be improved across Europe, through proper reimbursement and endorsement of effective therapies by national health care systems.

Dedicated resources are needed at national level to ensure that all patients screening positive for hepatitis B markers are offered the best care possible across all health care settings.

D². Dedicated resources towards hepatitis B

- National governments should allow for sufficient resources and funding of care, services and treatment for hepatitis B to allow best practice guidelines to be implemented fully
- All persons who have screened positive for Hepatitis B virus must be guided towards appropriate case management, which should include counselling and information about risks of transmission, protective measures to be taken to protect their household and sexual contacts and management of the disease
- Information on all treatment options available should be readily available and communicated by trained personnel regardless of the setting of care

D³. European clinical guidelines

- Clinical Practice Guidelines that encompass prevention, treatment and monitoring of hepatitis B are currently being developed by the European Association for the Study of the Liver (EASL) and will be available by early 2008^{19, 20}
- National centres of excellence in liver disease should translate these guidelines into clear treatment algorithms to be communicated across health professional teams to ensure *consistency of treatment to the highest standard* for all persons infected with HBV

19. These guidelines are developed along similar lines to other scientific society guidelines, including AASLD (Lok et al, 2007) and are based on a systematic review of the literature and expert consensus.

20. A review of existing guidelines found relative consensus amongst guidelines but highlighted the need for these guidelines to be implemented in practice. In particular, they called upon 'clinicians, national health authorities and the pharmaceutical industry to act jointly and co-operatively' to ensure that treatment of chronic hepatitis B evolve in a way so as to prevent the creation of multidrug-resistant HBV disease and that cost-effectiveness evaluations help guide the selection of alternative treatments (Thomas et al, 2007).

- In particular, treatment algorithms should help address controversies such as:
 - when to initiate treatment
 - the appropriate choice of treatment
 - measurement of response
 - A multidisciplinary approach to patient management, recognising the psychological as well as the clinical dimension of the illness and its impact on patients, should be adopted in practice in all settings.

Treatment protocols and guidelines must recognise hepatitis B as a liver disease, as well as an infection, and encompass all aspects of the natural history of disease, from acute infection to cirrhosis and need for transplantation.

D4. Professional training

- Several studies have identified lack of training and understanding of hepatitis B by general practitioners and non-hepatology specialists in the community and hospital settings as a key hurdle to early detection and appropriate management of hepatitis B²¹
- *Training* on the symptoms and clinical management of hepatitis B should be offered to all general practitioners, primary care providers, public health nurses and doctors working in out-patient clinics to help them identify patients at risk and manage hepatitis B early to avoid it reaching chronic stages and complications
- Professionals should be encouraged to *inform patients about the full scope of treatment options* for hepatitis B and provided guidance and links to hepatology clinics for patient referrals²²
- Within hospitals, all staff, especially nurses, should be offered access to training and sensitivity awareness on hepatitis B
- Patients who do not comply with proposed treatment regimens should receive support from specialised nurses to explain the importance to delay progression of disease to cirrhosis and advanced fibrosis to reduce the risk of getting liver cancer

Relevant national ministries with the support of advocacy groups should develop dedicated training programmes for all relevant health care professionals, hospital - as well as community-based, on the prevention, detection and clinical management of hepatitis B.

21. TNS NIPO Survey of June 2007 – International study to measure awareness, knowledge and problem recognition of healthcare professionals

22. In addition, the EASL (European Association for the Study of the Liver) has recommended the creation of a subspecialty in hepatology to be adopted across Europe, following on from the example of the British Association for the Study of the Liver's success in obtaining recognition of this sub-specialty in 2003. Their rationale is that such a specialty is necessary to improve standards of care for patients with hepatitis B. The EASL has designed a Training Curriculum which may be adapted to national curricula (EASL, weblink: www.easl.ch).

D⁵. EU research funds towards innovative hepatitis B treatments

- EU funding is already made available, under the EU Seventh Community Framework Programme dedicated to Research (FP7), to projects focusing on the development of new therapies, diagnostic tools and preventive tools addressing hepatitis co-infection will receive EU funding.²³ This scope should be broadened *to provide funding for hepatitis B treatments and resistance to antivirals in their own right*, regardless of whether co-infection with HIV exists
- The EU should ensure in its funding that projects are *not limited to improving access to selected risk groups* at the expense of others. For example, a Project funded under the previous Community Framework Programme (FP6) was dedicated to improving access to treatment for people with drug related problems. Such programs should be extended to other risk groups as well²⁴

EU research funds should be dedicated to the study of innovative treatments for hepatitis B and resistance to antivirals and not be limited to co-infection with HIV. Treatment options should also be advocated for all persons suffering from hepatitis B and not restricted to given groups.

D⁶. Support from advocacy groups

- Primary care and hospital clinics should make available to every person receiving a positive diagnosis of Hepatitis B the contact information of organisations where they may seek information on treatment and *support throughout the course of their illness*²⁵
- *Patient advocacy groups* should continue to support people infected with HBV and encourage them to take control of their conditions and seek appropriate care at every stage of their illness

Advocacy groups should be consulted by their national Ministries of health to ensure that patients who receive a positive diagnosis of hepatitis B infection are provided with comprehensive information about 'how to live' with hepatitis B, including treatment options

23. 18 September 2007 – FP7 Calls for Proposals – Hepatitis: http://ec.europa.eu/research/health/poverty-diseases/call-for-proposals_en.html

24. Project reference: 2005322 – started 01-12-2006 and has a duration of 36 months: http://ec.europa.eu/health/ph_projects/2005/action3/action3_2005_22_en.htm#3

25. For example, the Hepatitis B Foundation UK provides information on treatment options as well as more general information about hepatitis B (www.hepb.org.uk).

3. Conclusions

This document has issued a number of recommendations that need to be taken forward to ensure that the burden posed by hepatitis B across Europe is minimised over years to come. The most salient recommendations are:

- The EU should play a leading role in recognising hepatitis B as a significant public health problem and developing a cohesive strategy to ensure its proper prevention, control and management across Europe
- This strategy should then be implemented at national levels across the EU and beyond
- Europe should follow the WHO recommendations on vaccination and adopt a uniform policy of universal vaccination of all infants and adolescents
- Better information is needed for health professionals, the general public and groups at risk of infection from the hepatitis B virus to ensure that appropriate preventative measures are adopted and that those infected are guided to appropriate treatment options
- Targeted efforts are needed to prevent the spread of hepatitis B particularly in prisoners, injection drug users and immigrants
- European-wide surveillance of hepatitis B cases, both acute and chronic, is urgently needed to allow for the full burden of illness to be ascertained and effective policies to be introduced where they are needed most
- Sustainable funds are needed at national level to ensure that all persons affected by hepatitis B receive the highest standards of care available
- Access to therapies must be improved as they play a significant role in reducing avoidable deaths and help to prevent a further spread of the disease
- Training of all health professionals is needed to ensure that treatment guidelines are implemented and patients are offered the full spectrum of prevention, screening and treatment options throughout the course of their disease
- Basic and clinical research should be encouraged and funded at the European level in order to improve our understanding of the disease, its natural history and complications, to improve current care and develop innovative therapies

4. Glossary of terms²⁶

Acute Hepatitis Infection: A new, suddenly occurring infection. It occurs with a person's first exposure to the hepatitis B virus.

Antibody: A protein molecule produced by the immune system in response to a foreign body, such as the hepatitis B virus. Antibodies can be produced in response to a vaccine or to a natural infection. They circulate in the blood to protect against future infections.

Antigen: A protein on the surface of a virus, bacteria or cell that can stimulate the immune system to produce antibodies as a defense mechanism.

Asymptomatic: Refers to infection or disease without signs of illness. Many patients with hepatitis B do not have any symptoms during a new or chronic infection; they are considered to be asymptomatic.

Bloodborne Pathogens: Substances present in the blood that can cause infection or disease. Hepatitis B and hepatitis C viruses are bloodborne pathogens since they are spread through blood and can cause a liver infection.

Call for Action: A Call for Action is a document composed by an MEP (or a number of MEPs) calling the European Commission or other EU bodies (including Member States) to take action on a given subject. Additional MEPs are asked to sign the document to give further weight to the request.

Chronic Hepatitis B Infection: A patient who tests positive for the hepatitis B virus for more than 6 months is considered to have a chronic hepatitis B infection.

Cirrhosis: Irreversible scarring of the liver, due to ongoing damage, which may affect liver function. Cirrhosis can lead to liver failure and even death.

DG Sanco (Health and Consumer Protection): The European Commission's sector for health, which is headed by Commissioner Markos Kyprianou.

ECDC: The European Centre for Disease Prevention and Control (ECDC) is an EU agency that has been created to help strengthen Europe's defenses against infectious diseases. The ECDC's mission is to identify, assess and communicate current and emerging threats to human health posed by infectious diseases.

European Commission: The European Commission (formally the Commission of the European Communities) is the executive body of the European Union. Its primary roles are to propose and implement legislation, and to act as 'guardian of the treaties' which provide the legal basis for the EU. The Commission is divided into separate Directorate Generals (DGs) specialising in different policy areas.

European Council: The European Council is a part of the political infrastructure of the European Union which meets around four times a year. It comprises the heads of state or government of the Union's member states along with the President of the European Commission. Member States of the EU take turns in the Presidency of the European Council on a rotating basis, in sixth month long periods. Its main role is to provide broad aims and guidance on the direction of the European Union.

EU Blood Safety Directive (2002): The EU Directive which sets standards for quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components.

European Parliament: The European Parliament is the directly elected parliamentary body of the European Union. There are 785 elected members, MEPs, working within the European Parliament representing 27 member states. The Parliament does not have the power of legislative initiative; this belongs to the European Commission. Instead the European Parliament can develop and refine, or reject, the Commission's proposals.

European Parliament Resolution: A text adopted by the European Parliament embodying its opinion either on a legislative text – a 'legislative resolution' – or on any subject chosen on Parliament's own initiative – a 'non-legislative resolution' – with the intention of influencing a given European Union policy.

EU Seventh Community Framework Programme dedicated to Research (FP7): The Seventh Framework Programme for research and technological development (FP7) is the European Union's chief instrument for funding research over the period 2007 to 2013. It bundles all research-related EU initiatives together under a common roof playing a crucial role in reaching the goals of growth, competitiveness and employment.

EuroTransplant: The Eurotransplant International Foundation is responsible for the mediation and allocation of organ donation procedures in Austria, Belgium, Croatia, Germany, Luxembourg, the Netherlands and Slovenia. In this international collaborative framework, the participants include all transplant hospitals, tissue-typing laboratories and hospitals where organ donations take place.

'Health in all policies' principle: The 'Health in all policies' is a term used during the Finnish Presidency of the European Council in 2006. It proposes that health is largely determined by factors outside the domain of health care. The principle aimed to improve the health of the EU's population through coherent action in sectors other than health sector. This principle has also been adhered to in a great deal of EU health policy discussions since the Finnish Presidency ended.

Hepatitis: Refers to "inflammation of the liver", which can be caused by many things such as viruses, bacterial infections, trauma, adverse drug reactions, or alcoholism. Inflammation of the liver caused by viruses is called "viral hepatitis".

Hepatitis B Blood Panel: There are three common hepatitis B tests that make up the Hepatitis B Blood Panel (Hepatitis B Surface Antigen (HsAg), Hepatitis B Surface Antibody (HBsAb or anti-HBs) and Hepatitis B Core Antibody (HBcAb or anti-HBc). The Blood Panel is a simple test that requires only one blood sample, which can be obtained during an office visit to the doctor.

Hepatitis B Surface Antigen (HBsAg): The surface protein of the hepatitis B virus that is used as a marker to detect infection. If this blood test is positive, then the hepatitis B virus is present.

Hepatocellular Carcinoma (HCC): A malignant tumor of the liver, otherwise known as liver cancer. Chronic hepatitis B and C infections may increase the risk of developing liver cancer.

Hepatologist: A doctor who specialises in the study and treatment of liver disease. Ideally, patients with chronic hepatitis B or C should see a "hepatologist".

Member States: Member States refers to the 27 countries that are a part of the European Union.

Virus: A tiny microorganism, smaller than bacteria, which can invade the body and cause disease. A virus can reproduce itself exactly or mutate and make small changes. The ability of a virus to change slightly in each infected person is why treatment of viral diseases is so difficult.

WHO: The World Health Organization (WHO) is a specialised agency of the United Nations (UN) that acts as a coordinating authority on international public health.

2003-8 EU Public Health Programme: The European Parliament and European Council adopt strategic public health programs periodically to create an integrated approach towards protecting and improving health in the EU. On 23 September 2002, the European Parliament and the Council adopted a new Community action programme for public health. This programme runs for a 6 year period (from 1 January 2003 to 31 December 2008). The programme is based on three general objectives: health information, rapid reaction to health threats and health promotion through addressing health determinants.

26. For a full glossary of clinical terms associated with hepatitis B, please refer to <http://www.hepb.org/hepb/glossary.htm>.

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6. Appendix 1

Participants in the Hepatitis B Expert Meeting at the European Parliament, 3 July 2007

Chair:

Dr. Thomas Ulmer MEP, European Parliament

Moderator:

Charles Gore, ELPA and Hepatitis C Trust UK

Participants:

Mrs. Albená Arnaudová, WHO

Mr. Ronald Haigh, expert contribution

Mrs. Corinne van Lingen, Dutch permanent representation to EU

Prof. Michael Manns, Director Dept. of Hepatology, University of Hanover

Prof. Angelos Hatzakis, Hellenic Centre for Infectious Diseases Control

Prof. Stephanos Hadziyannis, Athens University School of Medicine and Henry Dunant Hospital of Athens

Prof. Andrzej Horban, Director Infectious Diseases Hospital, Warsaw

Prof. Howard Thomas, Imperial College, London

Prof. Liliana Preotescu, Institute of Infectious Diseases, Bucharest

Prof. Nurdan Tözün, Marmara University and Turkish Association for the Study of the Liver

Penny Webb, Hepatitis B Foundation UK, Coordinator

Dr. Suzanne Wait, Director of Research, International Longevity Centre-UK

Sebastian Rohde, Rohde Public Policy, Brussels, Belgium

Anouk De Vroey, Bristol-Myers Squibb EMEA, Belgium

Karine Ghesquire, Bristol-Myers Squibb EMEA, France

Jamie Griffin, Bristol-Myers Squibb EMEA, France

7. Appendix 2

List of experts who provided input in addition to participants (appendix 1)

Prof. Dr. Solko Schalm, Liverdoc, Erasmus University Rotterdam

Prof. Pierre Van Damme, University of Antwerp, Centre for the evaluation of vaccination.

Dr. Alex Vorsters, University of Antwerp, Viral Hepatitis Prevention Board

Prof. Jean-Michel Pawlotsky, Director, French National Reference Center for Viral Hepatitis B, C and delta

Nadine Piorkowski, President ELPA

Jos Draijer, Health attaché, Dutch Permanent Presentation to EU

Prof. Jacques Scheres, University of Maastricht, Member of the Board of the ECDC

Prof. Giampiero Carosi, Infectious Disease, University of Brescia, Italy

For further information on this report, please contact:

Dr. Thomas Ulmer MEP

European Parliament

Rue Wiertz

B 1047 Brussels

thomas.ulmer@europarl.europa.eu