

SHINING A LIGHT *on a* HIDDEN EPIDEMIC

Why and How Civil Society Advocates Can Support
the Expansion of Hepatitis C Treatment
in Eastern Europe and Central Asia



ACCESS TO ESSENTIAL MEDICINES INITIATIVE

 OPEN SOCIETY INSTITUTE
Public Health Program

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Jeff Hoover

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Cover Photograph by Matt Curtis | Open Society Institute, 2007. Activists at a harm reduction conference in Ukraine express frustration over access to health care, asking, “Why don’t they hear us?”

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Public Health Program

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Executive Summary

The hepatitis C virus (HCV) represents a serious health threat to people around the world. Some 150 million individuals are currently living with the virus and an additional three to four million people become infected every year. HCV can cause debilitating and fatal liver disease in approximately 25 percent of chronically infected people. Responding to the virus can be challenging for numerous reasons, notably in regards to treatment effectiveness and access. Treatment options are limited, response rates are suboptimal, side effects can be incapacitating and costs are prohibitive.

HCV's impact is particularly devastating in Eastern Europe and Central Asia. One main reason is that HCV infection is strongly correlated with injection drug use. In Russia and Ukraine, by far the two most populous countries in the region, there are perhaps 2 million and 400,000 injection drug users (IDUs), respectively, which put the two countries among the world's highest in terms of drug-using prevalence. Drug users experience significant discrimination wherever they live, but both the scale and degree of stigmatization are exceptionally pervasive across the former Soviet Union. Authorities and policymakers have long ignored or repressed people they consider disposable, such as drug users. They are frequently denied access to the full range of services—health, legal, or social—that are available to their fellow residents. As a result, HCV and other deadly diseases associated with stigma and marginalization, notably HIV, are spreading throughout society.

Awareness regarding HCV is largely nonexistent in the region, even among most IDUs. That stems at least in part from—and in turn reinforces—a lack of access to most aspects of HCV-related care, from diagnostics to treatment to managing side effects. The high cost of treatment is a key factor. Only two versions of pegylated interferon—one of the two medicines that together comprise the most effective HCV treatment—are currently available in most of the world. Both versions are brand-name drugs and are protected by patents nearly everywhere. Given the lack of competition, neither company has much incentive to lower prices; therefore, a course of treatment can cost more than \$20,000. That price is out of reach for many patients even in the world's richest countries where all or the majority of individuals are covered by insurance schemes and/or generous public-sector health systems. Unsurprisingly, most of the few patients in Eastern Europe and Central Asia receiving treatment for HCV infection only have access to substandard regimens.

The estimated 10 million people currently living with HCV in the region deserve better. All stakeholders must understand that inattention to HCV issues has already had serious individual and public health consequences that directly affect efforts to prevent and treat a host of other conditions, including HIV and drug dependence. The situation will only get worse if HCV does not receive the attention it deserves in the future. Unfortunately,

there is little indication that policymakers will take such a step on their own: instead, initial responsibility rests with civil society, especially groups comprising people living with HCV and members of vulnerable populations, such as drug users. This points to the overarching recommendation of this paper: NGOs in the region should build their capacity to advocate around all issues related to HCV.

All obstacles to comprehensive HCV treatment and care ultimately must be addressed, but, as this paper also argues, a priority emphasis should be placed on improving access to high-quality, affordable HCV treatment. This will not be easy. For one thing, no new medicines to treat HCV are likely to be available anywhere in the world for several years. Therefore, an immediate focus of advocates, public health officials, and policymakers worldwide—including those in Eastern Europe and Central Asia—should be on expanding access to the best option currently available: dual therapy involving ribavirin and pegylated interferon. This will require directly addressing the main barrier: the high cost of pegylated interferon.

Patient advocates and their allies in many parts of the world have begun seeking to overcome this barrier in a number of complementary ways. The main strategy is to encourage and help facilitate production of generic pegylated interferon—preferably more than one version to ensure even greater competition and the lowest possible prices. This strategy ultimately proved successful in regards to HIV drugs. HCV treatment must be approached in the same way: by developing and making available safe, effective, and cheaper generic versions of existing brand-name medicines and increasing research into the creation of new, less expensive therapies.

As noted in this paper, successful efforts already have been made in parts of the world (such as Egypt) to develop and distribute lower-priced HCV medicines in order to reach larger numbers of those in need. Similar steps could be taken in Eastern Europe and Central Asia. At least two of the region's nations, Russia and Ukraine, have relatively sophisticated domestic pharmaceutical manufacturing capacity. If HCV therapy development were a priority—and a case can certainly be made for it to be so, given the current public health situation—officials at domestic drug companies and government policymakers could conceivably collaborate in an effort to stem the looming crisis and help improve access to HCV treatment worldwide. Civil society groups could help support these efforts through targeted advocacy and monitoring.

Another approach that might prove even more successful would be to forego domestic production in the region and focus on sourcing generic HCV drugs, particularly pegylated interferon, from developing countries with stronger traditions of generic drug manufacturing. India and China are perhaps the most obvious examples. Pharmaceutical companies in both nations have extensive experience in developing and exporting safe,

effective generics. Under international trade rules, countries in Eastern Europe and Central Asia could issue compulsory licenses and then legally purchase generic HCV drugs from those countries—including pegylated interferon, once it is produced. Global sourcing HCV medicines in this way would quite possibly be quicker and less costly than initiating and ramping up production in the region.

This paper proposes a series of recommendations intended to expand and improve access to HCV services across the region. All support the top priority: the need to build HCV-specific civil society awareness and advocacy in the region. They should be considered complementary recommendations to be acted upon simultaneously. A summary of the recommendations is listed below. Each is discussed in greater detail in Section 8 of the report.

1. Recommendations regarding HCV surveillance, awareness, and testing

- Government agencies and civil society should collaborate in devising, implementing, and monitoring the effectiveness of expanded efforts to gather data and surveillance on HCV prevalence and trends.
- Government agencies and civil society should collaborate in devising, implementing, and monitoring the success of extensive HCV awareness campaigns. Campaigns must also target individuals living with HCV. Greater knowledge and support may increase their ability and inclination to i) avoid potentially risky behaviors that could transmit the virus to others, and ii) take other health-promotion measures, such as reducing alcohol intake, that can help ease stress on their livers. (Civil society would play a crucial role in such efforts because IDUs and members of other vulnerable groups often distrust or fear government entities based on real or perceived instances of discrimination and harassment.)
- All health care facilities should provide HCV diagnostics free of charge to all who want or need a test.

2. Recommendations to expand access to affordable HCV treatment

- Government officials and domestic pharmaceutical companies in the two most populous nations in the region—Russia and Ukraine—should collaborate to consider the possibility of developing, supporting, and sustaining the production of safe and effective generic versions of pegylated interferon.

- Civil society advocates and government officials in Eastern Europe and Central Asia should explore the possibility of global sourcing from outside the region. They should conduct adequate research in advance to identify the most logical, affordable, and cooperative partners as well as understand the complex global trade and patent issues involved.
- Government officials and policymakers in the region should exercise far greater political will and commitment to override patents and take other similar measures to make much-needed medicines more affordable on the domestic market, especially for public health systems. A major obstacle has been longstanding assumptions among Russian officials and many domestic patient advocates that generic medicines are by nature inferior to brand-name drugs. That may have once been true in the region, but it need not be if adequate monitoring and safeguards are put in place. Plenty of evidence is available showing that generic drugs for most conditions, including HIV, are safe and effective.
- Government officials—ideally from health care agencies—from across the region should establish a formal working group to facilitate inter-regional cooperation in improving access to HCV treatment. At least one civil society representative from each country should participate as well.
- Health care officials and medical personnel should commit to providing only the highest quality HCV treatment: combination therapy with ribavirin and pegylated interferon.
- Health care officials, civil society partners, and patient advocacy groups should explore in greater detail the possibility of using Global Fund programs to pay for HCV diagnostic and treatment services.

3. Recommendation to guarantee equity in HCV services access

- IDUs must be guaranteed equal and full access to all HCV-related services, including treatment.

About this Publication

This report provides the rationale and potential action steps to increase development of and broaden access to affordable, effective treatment for the hepatitis C virus (HCV) in Eastern Europe and Central Asia. To that end, it discusses and summarizes the following topics:

- Basic information about HCV, including its health impact and major transmission modes (Section 2)
- HCV diagnostics (Section 3)
- HCV prevalence (Section 4)
- HCV treatment regimens and their relative effectiveness (Section 5)
- Current access to, and prices of, HCV medicines and diagnostic tests in the region (Section 6)
- HIV–HCV coinfection (prevalence, natural history and treatment issues), progress toward developing effective generic medicines, and obstacles hindering drug users’ access to treatment (all side boxes).

The report concludes with a detailed analysis of why and how the capacity and engagement of civil society in HCV advocacy should be increased (Section 7), followed by specific recommendations (Section 8) for government policymakers, pharmaceutical companies in the region, and other HCV treatment advocates and their allies.

This report is not written by or for medical professionals, scientists, or health care providers who specialize in HCV diagnostics, treatment, and care. Instead, it seeks primarily to raise awareness about a growing health crisis in the region and to energize proactive advocacy and policymaking among patients, civil society groups, government officials, multilateral organizations and funding mechanisms (such as the Global Fund), and the pharmaceutical industry.

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Notes on Text

- For the purposes of this report, “Eastern Europe and Central Asia” refers to the 15 independent nations that were once part of the Soviet Union.
- All figures marked with “\$” are U.S. dollar amounts.

1. Introduction

There is little doubt that the hepatitis C virus (HCV) represents a serious health threat to people around the world. Some 150 million individuals are currently living with the virus and an additional three to four million people become infected every year. HCV can cause debilitating and fatal liver disease in approximately 25 percent of chronically infected people. Responding to it effectively—in regards to prevention, diagnosing and treatment—is challenging for numerous reasons. Among them are the following:

- The majority of people infected with HCV are not aware of their condition because only 20 percent experience symptoms when they become infected; some may not experience symptoms until years later. People who are unaware that they are infected with HCV do not seek medical care for the condition and do not take appropriate measures to prevent transmission to others.
- It is difficult to assess the extent of HCV-related liver damage without performing expensive and invasive tests.
- Treatment options are limited, response rates are suboptimal, cost is prohibitive and side effects can be debilitating. Access to potentially helpful medicines therefore ranges from nonexistent to scarce in most parts of the world.

Cases of this blood-borne infection have been recorded in every country. Yet even though higher prevalence has been recorded elsewhere, HCV's impact already is particularly devastating in Eastern Europe and Central Asia. One main reason is that the health, social and economic factors that strongly correlate with HCV infection in the region—notably, poverty and marginalization—are similar to those linked with HIV, another potentially deadly virus.

Current and former injecting drug users (IDUs) comprise the majority of people living with both HIV and HCV in nearly every country of the region, including the two most populous (Russia and Ukraine). Drug users experience significant discrimination wherever they live, but both the scale and degree of stigmatization are exceptionally high across the former Soviet Union. They are frequently denied access to the full range of services—health, legal or social—that are available to their fellow residents, even though constitutions and official policies in many countries specifically guarantee all citizens equal rights.¹

¹ Exceptionally high rates of drug use mean that diseases that disproportionately affect IDUs are particularly grave public health threats across much of Eastern Europe. In Russia and Ukraine, there are perhaps 2 million and 400,000 IDUs, respectively, which puts the two countries among the world's highest in terms of drug-using prevalence. Drug-use rates continue to climb, albeit from lower levels, in much of Central Asia.

Policymakers and government officials ignored HIV epidemics for many years, precisely because infections were concentrated among IDUs. Along with sex workers and men who have sex with men (MSM), drug users have long been treated harshly—if recognized at all. They are still largely considered disposable members of society, but evolving circumstances have essentially forced officials at all levels to moderate their ignorance and hostility. Policies are changing because HIV infections are becoming more common outside of drug-using communities, especially among young women, and it is increasingly impossible to deny or dismiss the devastating health and social impacts of surging HIV epidemics—including rising numbers of AIDS deaths.

As a result, tens of thousands of people in need now have access to antiretroviral treatment (ART) and effective prevention programs have been launched in many places, often at the instigation of local authorities who see the terrible consequences up close. Such hopeful developments are by no means as thorough as they should be, and HIV epidemics continue to surge throughout much of the region. However, recent positive steps nevertheless offer great hope for slowing or even reversing the spread of HIV across the region.

In comparison, the situation regarding HCV has barely budged over time. Lingering stigma regarding drug use and drug users remains one of the problems, but it is not the only one. The following are equally important issues that serve to limit responses to HCV not only in the region, but worldwide:

- HCV is poorly understood in comparison with HIV in terms of reasonably adequate surveillance data, transmission risks, and factors influencing disease progression.
- HCV disease progression usually takes decades, if it happens at all—with the important exception being that progression tends to be more common and quicker among people coinfecting with HIV.
- The recommended standard HCV treatment regimen is prohibitively expensive and has a high failure rate.
- The level of knowledge in the community about HCV standard of care treatment tends to be far lower in comparison with HIV treatment, a situation that increases distrust, fear and confusion among both patients and caregivers.
- Advocacy and awareness regarding HCV lag far behind that of HIV, even though four times as many more people around the world are estimated to be infected with HCV. As a result, the number of civil society and community groups focusing on HCV is just a fraction of those that work on HIV, a gap that persists in all parts of the world.

These obstacles are daunting, but they should no longer be used as excuses to do nothing. It is heartening to see that a growing number of activists across the region, many of whom have long-time experience working on HIV-related issues, are now turning their attention more directly to HCV. They deserve and need support from other advocates, particularly those affiliated with civil society groups that focus on health issues in general. Increased engagement of civil society is important because advocates can help make the case that failure to respond to HCV could lead to a public health crisis as significant as that posed by HIV.

Moreover, given the linkages between the two epidemics, it is clear that both should be addressed simultaneously and equally aggressively. The need to take such an approach is underscored by the fact that in countries with universal access to HIV treatment, including those in much of Western Europe, HCV is a leading cause of death among people living with HIV. HCV mortality rates among HIV-positive individuals are likely to increase as well in Eastern Europe and Central Asia.

Box A.

Deflated Hopes: Hepatitis Discussion Shelved at 2009 World Health Assembly

The persistent challenges advocates and organizations face in raising awareness about HCV were encapsulated by events at the annual World Health Assembly held in Geneva, Switzerland in May 2009. The original agenda called for discussions about hepatitis and other debilitating but often overlooked conditions such as Chagas disease. Advocates were particularly pleased by a Brazilian initiative to introduce a resolution on hepatitis that would, among other things, seek to enhance HCV prevention and control with WHO guidance and civil society involvement; commit governments to establish national HCV programs; call on UN agencies and other international organizations to provide more guidance, technical assistance and resources; and specifically mention the possibility of using flexibilities in global trade laws to increase access to HCV medicines and diagnostics.

Soon after the meeting began, however, organizers announced that it would be shortened to five days from nine to enable officials to return home to deal with growing concern about H1N1 ("swine flu"). Hepatitis was among the topics shelved; instead, it was announced that a resolution on viral hepatitis would be discussed at the WHO Executive Board meeting in 2010.

Many advocates were angered by the decision. Some noted, for example, that although H1N1 is a serious concern, it had infected less than 100,000 people around the world by that time and did not appear to be approaching pandemic status. In comparison, some 500 million people are living with hepatitis.

1.1 Priority Emphasis: Reducing the Cost of HCV Treatment

Access to most aspects of HCV-related care, from diagnostics to treatment to managing side effects, is limited across much of the region. All obstacles ultimately must be addressed, but this paper focuses on one major barrier that can conceivably be overcome through objective, quantifiable measures: the cost of treatment.

The current standard of care for hepatitis C consists of two medicines taken in combination: ribavirin and pegylated interferon. Generic versions of ribavirin are available, but for years pegylated interferon has been available only in two brand-name versions: Pegasys, made by Roche, and Schering-Plough's PegIntron. The lack of generic alternatives means that a standard 48-week course of treatment for HCV infection can cost more than \$20,000 even in resource-constrained countries such as those in Eastern Europe and Central Asia. As a result, most health systems are either unable or refuse to pay for the highest-quality HCV treatment for the majority of patients in need.

Patient advocates and their allies are seeking to overcome this barrier in a number of complementary ways. The main strategy is to encourage and help facilitate production of generic pegylated interferon—preferably more than one version to ensure even greater competition and the lowest possible prices. This strategy ultimately proved successful in regards to HIV drugs. HCV treatment must be approached in the same way: by developing and making available safe, effective, and cheaper generic versions of existing brand-name medicines and increasing research into the creation of new, less expensive therapies.

As discussed in this paper, successful efforts already have been made in parts of the world (such as Egypt) to develop and distribute lower-priced HCV medicines in order to reach larger numbers of those in need. Similar steps could be taken in Eastern Europe and Central Asia. At least two of the region's nations, Russia and Ukraine, have relatively sophisticated domestic pharmaceutical manufacturing capacity. If HCV therapy development were a priority—and a case can certainly be made for it to be so, given the current public health situation—officials at domestic drug companies and government policymakers could conceivably collaborate in an effort to stem the looming crisis and help improve access to HCV treatment worldwide. Civil society groups could help support these efforts through targeted advocacy and monitoring.

Another approach that might prove even more successful would be to forego domestic production in the region and focus on sourcing generic HCV drugs, particularly pegylated interferon, from developing countries with stronger traditions of generic drug manufacturing. India and China are perhaps the most obvious examples. Pharmaceutical companies in both nations have extensive experience in developing and exporting safe,

effective generics. Under international trade rules, countries in Eastern Europe and Central Asia could issue compulsory licenses and then legally purchase generic HCV drugs from those countries—including pegylated interferon, once it is produced. Global sourcing HCV medicines in this way would quite possibly be quicker and less costly than initiating and ramping up production in the region.

It is worth noting, too, that the time to strike is now. From a cost-benefit standpoint, the urgency to develop and distribute lower-priced HCV medicines is even greater in times of global economic crisis when health system budgets stagnate or decline. Improving and safeguarding the health of people living with HCV can have two important economic impacts: i) it ultimately lowers the cost and amount of medical care HCV-positive people will need, including care for severe liver disease, and ii) it contributes to an increase in social and economic productivity by helping individuals regain their strength and re-enter (or enter for the first time) the workforce. The second impact is further magnified when the increased productivity of caregivers—often family members of prime income-generating age—is taken into account.

2. Basic Background Information about HCV

The word “hepatitis” means “inflammation of the liver.” As a specific health condition, it usually refers to the impact of a series of viruses identified by letter (hepatitis A, B, C, etc.), each of which infects and subsequently “inflames” liver cells. The consequences of such inflammation can be extremely severe, if not life-threatening, because the body’s own immune response—to attack the infected cells—can cause scarring over time. Such scarring can in turn hinder or obstruct the liver cells’ normal activities, thereby reducing the liver’s ability to do its job properly. That development is dangerous because the liver is an organ that plays a critical role in filtering out bodily waste and regulating a wide range of essential biological functions.

As of early 2009, a total of at least five distinct versions of hepatitis had been identified.² All are potentially dangerous, but there are differences in modes of transmission, availability of preventive vaccines, common symptoms, short- and long-term health consequences, and the type and effectiveness of treatment (if the strain can be treated at all). Far more is known about hepatitis A and B, the most common versions, than other strains.

Hepatitis C (HCV) was identified as a distinct strain just two decades ago, at the end of the 1980s. Its complexity and relative newness mean that researchers discover new information about this rapidly mutating virus on a regular basis. At least seven different genetic versions, known as genotypes, had been discovered by the beginning of 2009; they are numbered from 1 onwards. Genotypes 1 through 3 are found around the world, but genotype 1 is by far the most common. It accounts for some 60 percent of all HCV infections worldwide and makes up the majority of infections in Eastern Europe and Central Asia.³ Not only is it the most common genotype, but it is also the most difficult to treat because it is less sensitive to existing therapies and requires a longer course of treatment.

Vaccines have been developed to help prevent infection with hepatitis A and B. None currently exist, however, for HCV. Development of a preventive vaccine for hepatitis C has been challenging because the virus eludes the immune response and becomes a chronic infection in the majority of infected people.

² The existence of the following hepatitis strains is accepted and understood by nearly all researchers and experts: A, B, C, and E. Most also agree that other distinct strains, including D and G, also exist.

³ As per the Hepatitis C Trust, a London-based non-profit. See www.hepctrust.org.uk/hepatitis-c/The+hepatitis+C+virus.htm.

2.1 Means of Transmission

Like other blood-borne infections, HCV can be transmitted when infected blood enters another person's bloodstream through any type of contact. The most efficient means of transmission are through blood transfusions and contaminated injection equipment. As a result, people living with hemophilia and IDUs are disproportionately likely to have HCV in every country of the world. Infection through transfusion is far less common now that donated blood is screened for HCV in most (but not all) countries. Infection through contaminated injection equipment has remained a serious risk, however; in some nations, more than 80 percent of IDUs already have HCV.

Numerous transmissions have been reported by other means, including poorly conducted public immunization campaigns (see Box B). HCV can be transmitted from mother to unborn child when, for example, membranes are ruptured—which means that about five percent of infants born to HCV-positive mothers are themselves infected. Sexual transmission is also possible, but the specific mechanisms of that sort of transmission are not entirely understood and contracting HCV during sex is thought to be relatively rare. The risk is higher with any sex act that draws or involves blood, such as rough anal and vaginal intercourse and when a female partner is menstruating. As with HIV, a condom can help reduce risk of sexual transmission of HCV.

It is important to note that unlike HIV, HCV can live outside the body for a significant period of time. This greatly increases the risk of transmission through unsterilized medical, dental, manicure, pedicure, and tattooing equipment and the sharing of certain personal-hygiene materials such as razors.

Box B.

Unfolding Public Health Disaster: HCV in Egypt

HCV transmission remains strongly correlated with injecting drug use in Eastern Europe and Central Asia, but epidemics elsewhere in the world show a much wider range of transmission modes and risks. In fact, the highest HCV prevalence in the world—more than 15 percent of the population—is currently found in Egypt, where injection drug use rates are far lower.

Egypt's HCV epidemic stems from poorly run public immunization campaigns against schistosomiasis (also known as bilharzia), a potentially fatal water-borne disease that had long been endemic in the country. For decades through the 1980s, improperly sterilized needles and syringes were used and re-used to administer bilharzia vaccination shots.

HCV spread quickly as a result. Millions of people were unintentionally infected with the virus long before it was identified in 1989; today, as many as 30 percent of Egyptians between the ages of 30 and 60 have HCV. The majority of them are still not aware that they have HCV, largely because public awareness about the disease is low and testing access and availability are limited. Meanwhile, anti-HCV medicines are beyond the reach of many who have been diagnosed. The country's high poverty rate and health sector resource constraints mean that treatment is unaffordable for most, even though a lower-cost version of pegylated interferon, a key drug in the best-quality combination treatment regimen, is now produced domestically (see Box G).

2.2 Disease Progression and Health Consequences

HCV has two distinct phases, acute and chronic. The acute phase occurs immediately after infection and lasts for about six months. In a small share of individuals—about 15 percent or slightly higher—the hepatitis C virus is cleared from their bodies by their immune systems, usually within 6 months of infection. The remaining 75 to 85 percent or so are unable to clear the virus, and they develop chronic hepatitis. The only way the virus can be eliminated from their bodies is by treating hepatitis C directly.⁴

Symptoms are rare during the acute phase and extremely unpredictable during the chronic one. As with HIV, some people living with HCV experience few or no symptoms for years to decades, while others feel ill and weak from the moment they are infected. Symptoms vary widely by patient as well, and many of the most common—fatigue, depression, aches and pains, and forgetfulness—can have numerous causes.

⁴ See "Global state of harm reduction 2008: Mapping the response to global HIV and hepatitis C epidemics," published in 2008 by the International Harm Reduction Association. Available online in PDF format: www.ihra.net/Assets/582/1/GSHRFullReport.pdf.

The lack of clear and identifiable symptoms is a main reason that many health care providers fail to suspect HCV, leaving patients undiagnosed. Often caregivers either are poorly informed about the disease (which is especially likely in resource-constrained countries, including many in the poorer nations of the former Soviet Union) or they fail to recognize potential risk factors that would prompt more extensive consideration of the cause of symptoms. Patients, too, may not be comfortable disclosing symptoms or may feel the symptoms are not worth discussing for one reason or another. (Cost is another important factor limiting diagnosis in Eastern Europe and Central Asia. In most countries of the region, diagnostic tests for HCV are not covered by public health systems. Those most likely to have HCV, including IDUs, are disproportionately poorer than the general population and thus not able to afford even minor fees for tests.)

HCV is now recognized to be the world's leading cause of liver disease. Chronic HCV can lead to mild-to-serious liver scarring (cirrhosis) in approximately 25 percent of people; those with cirrhosis are at risk for life-threatening complications such as liver cancer and liver failure. As noted previously, hepatitis C also causes a host of other problems, known as extrahepatic (outside of the liver) conditions. Such conditions include cryoglobulinemia (a serious blood disorder), peripheral neuropathy (feelings of numbness and tingling, especially in extremities), and pruritis (severe itching).

Alcohol use, especially when excessive, can exacerbate the onset and severity of liver disease among HCV-positive individuals. This factor is of considerable importance in several countries of Eastern Europe and Central Asia where rates of alcohol use and abuse are above global and regional averages. Those rates are particularly high in Russia and are thought to contribute to the low average life-expectancy level among Russian men.

The overall health and prognosis of people coinfecting with HCV and HIV are significantly worse as well (see Box C).

Double the Trouble: HCV and HIV Coinfection

Given overlapping transmission modes, it is not surprising that many people infected with HCV are also living with HIV. Since coinfection with the two viruses is particularly common among IDUs, HIV-HCV coinfection represents a major public health problem in Eastern Europe and Central Asia, a region with high drug-using rates. According to a 2007 study by the Eurasian Harm Reduction Network, more than 50 percent of HIV-positive people seeking care were also infected with HCV in several countries in the region, including Estonia (80 percent), Latvia (61 percent), Russia (52 percent), and Ukraine (77 to 80 percent).

Living with two serious viruses is undoubtedly worse than just one, an assumption that is not just intuitive but has also been verified by data and observations. HIV infection reduces the likelihood that the body can clear out HCV on its own, and HCV-related disease progression (including development of cirrhosis and liver cancer) is faster among coinfecting individuals.

Coinfection can also limit the effectiveness of both HIV and HCV treatment. Although antiretroviral treatment (ART) for HIV infection can delay hepatitis C-related liver disease progression, HCV coinfection can complicate HIV treatment because it triples the risk for ARV-associated liver toxicity and may limit treatment options. In turn, HIV is associated with poorer HCV treatment outcomes. In the United States and Western Europe, where ART is widely available, end-stage liver disease from HCV has become the leading cause of non-AIDS related death among HIV-positive individuals. The same outcome can be expected in Eastern Europe and Central Asia if ART access is broadened without access to HCV treatment.

Such impacts are important to recognize, but they pale in comparison to the potentially negative consequences of not getting treatment for either or both HIV and HCV if the need becomes apparent. Simultaneous, joint treatment is by far the best option for numerous reasons, including the fact that HCV treatment has been found to improve tolerance of ART. The most effective HCV regimen—a 48-week course of ribavirin and pegylated interferon—is recommended for coinfecting individuals as well. Although certain HIV medicines should be avoided, the far wider range of treatment options for that disease usually means that a regimen can be cobbled together.

3. HCV Diagnostics

3.1 Testing for the Presence of HCV

First introduced in 1991, the HCV antibody test is used to determine if a person has ever been infected with hepatitis C. As with HIV antibody testing, blood samples are tested not for the virus itself but for the presence of antibodies generated by the immune system's response to the infection. However, in contrast with HIV, a positive HCV antibody test result does not always accurately indicate HCV infection.

For one thing, it is possible for an HCV antibody test on an infected individual to come back negative when he or she has been infected within six months. Tests usually come back negative with immuno-compromised persons, including transplant recipients and HIV-positive individuals with very low CD4 counts, because their immune systems are not producing HCV antibodies. Inaccurate readings can go the other way too. Since about 15 to 25 percent or so of people infected with HCV clear the virus from their body over time, they may test positive for HCV antibodies (which remain in the system), yet not actually be infected.

Confirmatory testing that looks for hepatitis C virus in a blood sample is therefore necessary to confirm or rule out HCV infection. Viral load testing is the most common method. This test detects the actual presence of HCV in blood as little as two weeks after infection. Where possible, people who believe they may have been exposed to HCV are urged to get a follow-up PCR test (a kind of viral load test)⁵ for confirmation after getting an antibody test.

PCR tests are undeniably more precise and accurate than antibody tests for detecting the presence of HCV. However, a PCR test is also a far more complex and expensive diagnostic procedure that requires higher-quality laboratory facilities and specially trained technicians. In many parts of the world, including much of the former Soviet Union, neither the expertise nor the funds are available to offer such tests in public sector health care systems.

⁵ PCR is an acronym for "polymerase chain reaction." PCR tests are described in greater detail in Section 3.2.

3.2 Other Important Diagnostic Tests

- **Viral load tests.** PCR tests can also play an important role after HCV infection has been confirmed. Not only do they detect the presence of HCV, but they also indicate the amount of virus in the patient's blood. A PCR test thus can measure what is known as the viral load, a key indicator that can help determine i) whether a patient is likely to respond to HCV treatment, and ii) whether HCV therapy has been effective in clearing the virus from the system of a patient already on treatment. Treatment is considered successful when viral load measurements decline over time and/or remain stable at extremely low or undetectable levels throughout the course of the treatment and six months afterwards

Two other tests are often used to measure HCV viral load in some parts of the world: branched-chain DNA and transcription-mediated amplification (TMA). The three tests vary somewhat in terms of precision, with the more sensitive test (PCR) being the most expensive to administer and evaluate. The TMA test is the newest and is considered by many experts to be the best option because it is reasonably sensitive and easier and cheaper to use than the other two tests.⁶

- **Genotype test.** Individuals who test positive for HCV and are considering treatment should also have their blood tested to determine which genotype they are infected with. This information is crucial because it will help determine the length of treatment and predict treatment response. For example, a 24-week course of treatment is most often given to (and proves successful for 80 percent of) people with genotype 2 or 3. Those with genotype 1, however, usually need to take a 48-week course of treatment—and the standard regimen proves successful only in about half of cases.⁷
- **Liver biopsy.** A liver biopsy is used to identify the cause(s) and extent of liver damage. A biopsy can gauge the amount of scarring (stage) and inflammation (grade) of a patient's liver. The test consists of inserting a needle into the liver and extracting a small piece of the organ, which is subsequently examined to measure the degree, if any, of damage and inflammation.

⁶ As per "HCV viral load tests," a fact sheet published in 2006 by the Hepatitis C Support Group. Available online in PDF format: www.hcvadvocate.org/hepatitis/factsheets_pdf/VIRALLOAD.pdf.

⁷ As per "HCV diagnostics tests," a fact sheet published in 2006 by the Hepatitis C Support Group. Available online in PDF format: www.hcvadvocate.org/hepatitis/factsheets_pdf/diagnostic_FS.pdf.

Liver biopsies may be recommended at five-year intervals to those with chronic, untreated or unsuccessfully treated HCV.⁸ They are also useful for patients who are undecided about treatment or suffer from other conditions (known as comorbidities) that put their overall health at risk. Caregivers are likely to strongly encourage such patients to put off treatment for several years if their liver biopsy results are normal or only mildly abnormal. It may be that their ability to tolerate treatment (especially the side effects) will improve over time or that more effective and less toxic agents will eventually be available for them.

In recent years, non-invasive procedures have been developed to help determine the health of a liver. The most common, known as ultrasound elastography, is undertaken with a device known as a FibroScan that is administered on the patient's abdomen. This method measures the stiffness of a liver, a reading that is useful because an unhealthy liver is firmer than a healthy one.

Other potentially important diagnostic tests, especially for those considering or undertaking treatment, are those that monitor treatment efficacy and toxicity. These diagnostic tests are important for ensuring the highest-quality care possible for people living with HCV. Without them, it is nearly impossible for caregivers to recommend appropriate treatment (if available) for HCV infection itself and for associated debilitating liver diseases, including liver cancer. All efforts to expand access to HCV treatment must therefore focus not just on medicines intended to eradicate the virus, but also on ensuring that a full suite of diagnostic tools and expertise to conduct and review them are available as well.

Comprehensive HCV treatment resources of this kind are currently available in public-sector health programs in only a few select places in Eastern Europe and Central Asia, most notably in the wealthier Baltic nations. The majority of those in need in the region, however, live elsewhere.

Availability does not necessarily lead to easy access, however. Even where one or more of these diagnostic tests are in fact available, they are not always provided free of charge. Prices vary depending on laboratory, health system and medical insurance scheme, but one advocate in the region estimated that in Ukraine, the average price in 2008 for a PCR test was \$80, with a genotype test priced at \$50.⁹

⁸ Ibid.

⁹ As per an estimate provided in January 2009 by a WHO staff member based in Ukraine.

A final important—albeit sobering—observation relevant to the region is that despite the many theoretical benefits of HCV diagnostic tests, they are not necessarily a high priority to many patients or their caregivers when treatment options are nonexistent or severely limited. In such cases, not knowing (even if based on willful denial) may be more comforting than having certain information that causes anxiety, stress and constant fear.

3.3 Notable Non-diagnostics Barriers to Identifying HCV

The relatively lengthy discussion in Sections 3.1 and 3.2 of HCV diagnostics clearly illustrates the complexities involved in identifying infection. Such difficulties are exacerbated by two issues that also negatively affect HIV detection and care: i) potential lack of patient follow-up, and ii) stigma and discrimination around key risk factors.

Because blood samples must be examined in specialized laboratories, the results of HCV antibody and PCR tests are not known for several days after blood is drawn.¹⁰ The delay means that a small but significant share of patients may not return to get their test results. Caregivers often are not able to reach them if, as in many cases, the tests are conducted anonymously or if patients do not provide accurate contact information for one reason or another.

The second issue is closely related to the first—especially in Eastern Europe and Central Asia, where HCV infection is particularly common among IDUs. Drug users often are unwilling or unable to seek out medical screening and care, including HCV and HIV tests, because they fear harassment or are concerned about violations of confidentiality. Also, because they tend to have little awareness or accurate information about HCV care in general, they may assume that drug side effects and toxicity greatly outweigh the potential benefits of HCV treatment.

¹⁰ Such a delay could be eliminated by the development and affordable pricing of a rapid test similar to the one now used increasingly to diagnose HIV infection. In fact, one company that pioneered a rapid HIV antibody test, OraSure Technologies, announced in mid-2007 that it had made significant headway in developing a test that could detect HCV antibodies in blood and saliva within minutes. More than a year later, in October 2008, the company submitted a premarket approval application to the U.S. Food and Drug Administration (FDA). The FDA had not responded by the time research for this report was completed in early 2009. (It is important to note, however, that a confirmatory viral load test is still needed to ensure an accurate HCV diagnosis. This means that a final, “certain” diagnosis still takes several days to obtain.)

This is, however, just one reason that the majority of people living with HCV in the region are not aware of their status. Another reason of perhaps even greater importance is lack of awareness about HCV among both health care providers and the general public. Even if caregivers have heard of the disease, they may know little or nothing about risk behaviors or symptoms. They are therefore unlikely to recommend that patients take an HCV test even if such tests are available and a patient seems to fit a profile suggesting he or she could have been exposed to the virus. Lack of awareness is equally problematic when viewed from the other side: limited awareness of HCV among IDUs and other vulnerable populations means that they are not likely to discuss it, let alone inquire as to whether a test is available, when in health care settings.

4. HCV Prevalence

Lack of awareness about HCV is common in most other parts of the world, not just in Eastern Europe and Central Asia. As a result, precise prevalence data are difficult to obtain. Recent estimates of cases of chronic HCV worldwide range from 140 million to 200 million;¹¹ in comparison, and to put the HCV crisis in perspective, the total number of people living with HIV is not thought to exceed 35 million.¹²

Of the HCV global total, an estimated 10 million people are living with chronic HCV across the former Soviet Union.¹³ That represents about four percent of the overall population in those 15 countries, prevalence higher than most estimates for the United States (slightly less than two percent) and Western Europe (about one percent or less in each country). Yet in some countries, notably Egypt (see Box B), more than 10 percent of the population is thought to be infected with HCV.¹⁴

As significant as some of these estimates are, they are dwarfed by prevalence estimates for certain high-risk groups in several countries. IDUs are especially susceptible to HCV because sharing of injection equipment, perhaps the most efficient transmission vector, regularly occurs among members of this population. HCV can be contracted by more than half of all individuals in a drug-using community within months of being introduced, especially in places where access to clean injection equipment is limited.¹⁵

¹¹ See, for example, "Global burden of disease (GBD) for hepatitis C," *Journal of Clinical Pharmacology*, 2004. Online: <http://jcp.sagepub.com/cgi/content/abstract/44/1/20>. Also, website of the Hepatitis C Trust: www.hepctrust.org.uk/hepatitis-c/.

¹² As per most recent global estimates from the Joint UN Programme on HIV/AIDS (UNAIDS). Online: www.unaids.org.

¹³ "Global burden of disease (GBD) for hepatitis C," *Journal of Clinical Pharmacology*, 2004. Online: <http://jcp.sagepub.com/cgi/content/abstract/44/1/20>.

¹⁴ At nearly 20 percent, Egypt's estimated HCV prevalence is the world's highest. Three other African countries are not far behind: Prevalence estimates top 10 percent in Burundi, Cameroon and Rwanda. See www.hepctrust.org.uk/hepatitis-c/.

¹⁵ See, for example, "Prevention of hepatitis C virus infection: Achievement through integration into established prevention programs," a PowerPoint presentation by Harold S. Margolis, M.D., Division of Viral Hepatitis, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, USA. Online: www.vhpb.org/files/html/Meetings_and_publications/VHPB_Meetings/geneva_2002/S4P3%20Margolis.ppt.

HCV prevalence among adult IDUs currently exceeds 50 percent in countries around the world, including some of the most populous. A recent report estimated that 92 percent of IDUs in India are infected with HCV, for example, as are 85 percent in Germany, up to 80 percent in the United States, and as many as 70 percent in Brazil.¹⁶

The situation is arguably worse in countries where a higher share of the population injects drugs, even if the absolute numbers of HCV-positive individuals currently are lower. Countries in this category include Thailand (where 90 percent of IDUs are thought to have HCV) and several in Eastern Europe and Central Asia. In Russia, for example, an estimated 90 percent of the country's 2 million IDUs have HCV; in Ukraine, meanwhile, between 70 and 90 percent of the country's 400,000 or so IDUs are living with HCV.¹⁷ HCV prevalence rates exceeding 50 percent of IDUs are also found in several other countries in the region, including Lithuania (95 percent), Estonia (90 percent), and Kazakhstan (66 percent).¹⁸

HCV represents a particularly dire public health threat in those nations because of the following reasons:

- HIV epidemics in these countries are concentrated among IDUs, which means that HIV-HCV coinfection is common.¹⁹
- Some have policies in place that specifically deny HCV treatment for IDUs.
- In comparison with many other nations, especially those elsewhere in Europe, they provide fewer and less comprehensive health services for IDUs in general (including appropriate and adequate harm reduction and drug treatment services).
- They have relatively limited financial or human resources in their health sectors in the wake of post-Soviet economic transitions.

¹⁶ See "Global state of harm reduction 2008: Mapping the response to global HIV and hepatitis C epidemics," published in 2008 by the International Harm Reduction Association. Available online in PDF format: www.ihra.net/Assets/582/1/GSHRFullReport.pdf.

¹⁷ See "Global state of harm reduction 2008: Mapping the response to global HIV and hepatitis C epidemics," published in 2008 by the International Harm Reduction Association. Available online in PDF format: www.ihra.net/Assets/582/1/GSHRFullReport.pdf.

¹⁸ Ibid.

¹⁹ For example, according to data obtained from laboratory tests in Ukraine (2006 and 2007), 82.4 percent of HIV-positive individuals were coinfecting with HCV, as were 94.8 percent of HIV-positive IDUs. Also of note from this study were findings that 61.5 percent of all IDUs, 61.1 percent of prisoners, and 46.7 percent of TB patients had HCV. (This information was contained in a chart titled "HBV and HCV infection markers in different population groups in Ukraine." The chart was compiled by T.A. Sergeeva at the L.V. Gromashevskiy Institute of Epidemiology and Infectious Diseases within the Academy of Medical Sciences of Ukraine.)

Box D.

Barriers to Treatment for Active Drug Users

Access to the current standard of care for HCV treatment is not easy or guaranteed for any individual in Eastern Europe and Central Asia. Some, though, face greater obstacles than others.

Active IDUs fare the worst for a variety of reasons. They are considered by the general public to be weak, shiftless, and irresponsible individuals who threaten social stability by continuing to break the law. Little sympathy is extended when they are harassed or have their legal, economic or social rights violated.

Such attitudes are common among health care personnel at all levels, including policymakers. Active IDUs are often denied health services based on the assumption that such care would be “wasted” on them. In recent years, official policies in some countries—including Belarus, Estonia, Lithuania, and Russia—have recommended or explicitly stated that abstinence from illicit drug use is a prerequisite for receiving treatment for HCV. In other nations, meanwhile, treatment has been routinely withheld from active IDUs even in the absence of official abstinence-only policies.

Supporters of such policies, official or not, often argue that active drug users are not capable of adhering to treatment regimens or that illicit drug use lessens adherence to, and effectiveness of, antiviral medicines. There is no evidence to support either of those assumptions. On the contrary, studies have shown that active IDUs can be as adherent as non-users, if not more so, to rigid treatment regimens such as those prescribed for HCV and HIV.

Other studies undermine another frequent rationale used by policymakers seeking to bar active IDUs from HCV (and, often, HIV) treatment: that the medicines and therapies are not as effective in active users. Nearly every study instead reports HCV treatment outcomes among active users that are comparable to those among people not using drugs.

Evidence indicates that adherence among active IDUs can be increased even further when they have complementary access to additional health and social services such as mental health care, non-coercive drug treatment programs, and harm reduction support (such as clean injecting materials and methadone or buprenorphine treatment). Specialized training can also make a big difference in improving health care workers' attitudes toward drug users, thereby turning them into supportive caregivers and valuable advocates on behalf of their patients.

Patients and advocates often find that evidence-based data and observations cannot overcome existing treatment barriers on their own, however. Also effective on occasion are appeals to basic equality and human rights. In this view, active drug users are no less deserving than anyone else in terms of obtaining access to services and support to improve their health.

IDUs in many formerly Soviet countries also tend to face more extensive abuse, harassment and discrimination when dealing with law enforcement and health authorities.²⁰

²⁰ See, for example, “Rehabilitation required: Russia’s human rights obligation to provide evidence-based drug dependence treatment,” a November 2007 report from Human Rights Watch. Online: www.hrw.org/en/reports/2007/11/07/rehabilitation-required-o.

5. HCV Treatment

5.1 Current Options and Standards

HCV treatment options currently are limited not only in number but in effectiveness. The contrast is particularly stark in comparison with HIV, a disease that was identified only a few years before HCV. More than 30 distinct anti-HIV medicines are currently used around the world, and lower-priced generic versions of many of those drugs are increasingly available in the countries where need is greatest. Some three million people with HIV now have access to potentially life-saving treatment. Much work still needs to be done to improve access in much of the developing world, including countries in the former Soviet Union where prices remain relatively high and treatment options are far too limited. But even so, it seems clear that improved HIV treatment access is a growing priority among most policymakers in the region.

Four times as many people around the world may have HCV than have HIV, but it would be extremely generous to assume that as many as four times *fewer* would have access to HCV treatment even if they needed it. The main reason: standard-of-care HCV treatment is extremely expensive. In all but a few places in the world, such treatment is unavailable to all in need, rationed to a select few, or purchased out of pocket by relatively wealthy individuals. Insurance schemes and public health systems rarely offer it to needy patients, either because they simply cannot afford to or because they choose to prioritize other diseases, many of which can be treated with cheaper medicines.

The current standard-of-care pharmaceutical treatment for HCV consists of combination therapy involving two drugs, ribavirin and pegylated interferon. That regimen has been recommended since 2001, the year pegylated interferon was approved by the U.S. Food and Drug Administration (FDA). The usual course of treatment lasts from 24 to 48 weeks, depending on genotype,²¹ with ribavirin taken daily (orally, in pill format) and pegylated interferon once a week (by injection). This regimen and all other HCV treatment options have significant shortcomings, however. Among them are the following:

- **They can have severe side effects.** Many people on HCV treatment abandon their regimens because they are no longer able or willing to tolerate side effects. Flu-like symptoms such as extreme fatigue and weakness affect many individuals; more debilitating side effects, including anemia, anxiety, and depression, are experienced by as many as one quarter of all patients. A large share are unable to work while

²¹ Treatment usually lasts for 48 weeks for those with genotype 1, which is most common in Eastern Europe and Central Asia, and half that time (24 weeks) for individuals with other genotypes.

on treatment because of the side effects. It is impossible for either patients or their caregivers to know in advance if (or what kind of) side effects from treatment might occur.

It can also be difficult to identify and prescribe therapies to mitigate the side effects and allow optimal treatment to continue. For example, anemia is relatively common among patients whose regimens include ribavirin. However, epoetin, the one drug known to effectively combat such anemia and allow the continuation of a ribavirin regimen, can have serious side effects of its own. It is also unavailable or unaffordable in many parts of Eastern Europe and Central Asia.

- **They have limited effectiveness.** Data indicate that the standard-of-care combination treatment (ribavirin and pegylated interferon) is only effective for slightly more than half of patients.²² Dual therapy involving ribavirin and non-pegylated interferon is even less effective (around 45 percent of patients),²³ and monotherapy (treatment with interferon only) is effective in one third of patients at best.²⁴ The percentages for each form of treatment are even lower for individuals coinfecting with HIV, especially those with low CD4 counts (see Box C).

“Effective” in the world of HCV treatment means that HCV is no longer detectable in an individual’s blood six months after treatment ends; this is known as a “sustained virological response,” or SVR.

- **They are extremely expensive.** Several generic versions of ribavirin are available around the world—which means that the medicine can be purchased relatively cheaply—but only two versions of pegylated interferon are on the market.²⁵ Both

²² It is important to note, however, that effectiveness as defined by this criterion differs by HCV genotype. About 80 percent of those with genotype 2 or 3 clear the virus with standard-of-care combination treatment (ribavirin and pegylated interferon), but success is much lower (at most 50 percent) for those with genotype 1. (As noted elsewhere in this report, the majority of HCV-positive people in the world, and in Eastern Europe and Central Asia, are infected with genotype 1.)

²³ As per the results, for example, of a large study released in 2004. See <http://eprints.soton.ac.uk/62113/>.

²⁴ Interferon monotherapy is sometimes provided when patients cannot tolerate ribavirin-specific side effects, most notably anemia. Ribavirin is not prescribed as monotherapy because it has no direct effect on HCV on its own.

²⁵ The two available pegylated interferons are not exactly the same because they use different types of molecules to prolong the half-life of the interferon. (The term “pegylation” refers to a process whereby a large molecule chain is attached to the interferon to slow the rate at which it is broken down.) They are also dispensed in different ways. Pegasys, made by Roche, is premixed and given at a fixed dose, while PegIntron, made by Schering-Plough, is dosed by weight and mixed prior to injection. See, for example, T Swan, “Research & policy recommendations for hepatitis C virus (HCV)/HIV coinfection: Critical issues from TAG’s forthcoming HCV/HIV coinfection report.” Treatment Action Group, New York, USA, February 2003. Online: http://img.thebody.com/legacyAssets/16/65/jan_febo3.pdf.

are brand-name drugs and very expensive. As a result, a course of combination treatment with pegylated interferon can cost more than \$20,000 in developed countries such as the United States. That price is out of reach for many patients even in the world's richest countries where all or the majority of individuals are covered by insurance schemes and/or generous public sector health systems.

The high-priced pegylated interferon duopoly persists for several reasons. Among them are the following: i) both medicines are patent-protected throughout much of the world, including in countries such as Russia and Ukraine, home to most HCV cases in Eastern Europe and Central Asia; ii) neither company has faced significant pressure from advocates or public sector purchasers to cut prices substantially; and iii) pegylated interferon is a complex and difficult product to manufacture because it is a so-called biologic, which means that it is derived from organic cells, not small chemical molecules.²⁶ (See Box E for a discussion of the difference between pegylated and non-pegylated interferon.) In many ways the current HCV treatment situation is similar to that in the HIV/AIDS world in the early 1990s, before mounting global pressure and patient advocacy opened the floodgates to new, lower-priced therapies that were equally effective as their branded counterparts.

Advocates in the region should be aware of and heartened by the fact, however, that their counterparts in some other developing countries are seeking to confront the duopoly. For example, efforts have been initiated in India to convince through negotiations—or force through legal measures—the manufacturers of the two brand-name pegylated interferon products to lower their prices. In 2007, an Indian NGO called Sankalp, which works to provide treatment and health services to IDUs, challenged a patent granted to Roche by the Indian Patent Office for Pegasys. That challenge followed a similar one filed two months earlier by a domestic drug firm, Wockhardt.²⁷ In April 2009, however, government patent authorities rejected the advocates' legal challenge and upheld Roche's patent. The decision was a setback, but some positive and hopeful signs can nevertheless be seen from the process. The advocates' challenge was supported by many public health officials as well as mem-

²⁶ The FDA's website includes the following thorough definition: "Biological products include a wide range of products such as vaccines, blood and blood components, allergenics, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins. Biologics can be composed of sugars, proteins, or nucleic acids or complex combinations of these substances, or may be living entities such as cells and tissues. Biologics are isolated from a variety of natural sources—human, animal, or microorganism—and may be produced by biotechnology methods and other cutting-edge technologies. Gene-based and cellular biologics, for example, often are at the forefront of biomedical research, and may be used to treat a variety of medical conditions for which no other treatments are available." See www.fda.gov/cber/faq.htm#3.

²⁷ See www.hepctrust.org.uk/news/2007/june/india-roches-hepatitis-c-drug-patent-challenged.htm.

bers of an intermediary panel whose anti-Roche recommendation was ultimately ignored by the patent authorities. Moreover, reports from India indicated that Wockhardt and at least one other generic drug company in that country, Shanta Biotech, would consider making generic versions of pegylated interferon if Roche's patent were overturned.

Box E.

Interferon: Indispensable, Complex, and Difficult to Manufacture

The standard of care for HCV is a combination regimen involving two medicines, ribavirin and pegylated interferon. Interferon is the backbone of HCV treatment, although it is much less effective when used without ribavirin.

About interferons. Interferons are natural proteins produced by the immune systems of humans and many animals in response to viruses and parasites. The medical compound known as “interferon” is based on those natural proteins and works in much the same manner, most notably by stimulating the immune system to fight viruses. Interferon is also used to treat some types of cancer, in combination with chemotherapy and radiation.

Man-made interferons are used in HCV treatment regimens to enhance naturally occurring interferons, which are not always able to prevent or fight HCV infection on their own. Interferon can cause serious side effects, many of which resemble flu symptoms (aches, fevers, shivering, fatigue, etc.). Interferon also suppresses bone marrow growth, which means it can cause potentially fatal conditions such as anemia. In addition, interferon can cause a range of debilitating non-physical problems ranging from anxiety to insomnia to depression.

About pegylated interferon. The term “pegylation” refers to a large molecule called polyethylene glycol—“peg”—that is attached to standard interferon. For reasons scientists have yet to fully understand, interferon with a “peg” molecule attached is more effective than standard interferon in clearing HCV. It is thought, though, that the molecule plays a role in keeping interferon from being broken down in the body, thereby ensuring the medicine is actively working for a longer period of time. It is also more convenient; pegylation reduces injections from three to one a week.

Pegylated interferon has been used as part of HCV treatment regimens for nearly a decade, since it was first approved by the U.S. Food and Drug Administration in 2001. Pegylated interferon is very expensive because manufacturing it is a complex process and developing safe, reliable and effective generic versions of pegylated interferon remains challenging. The eventual development of such versions would lead to much lower prices because of increased competition.

5.2 HCV Medicines in the Pipeline

More than 20 experimental HCV agents are currently in the pipeline at pharmaceutical companies worldwide. This means the compounds have at least been created with the goal of eradicating HCV or mitigating its effects and are currently undergoing, or being readied to undergo, clinical tests. The compounds range from medicines intended to mimic or replace existing HCV medicines—such as ribavirin substitutes and novel interferon formulations—to those that take a completely different approach to tackling HCV, including protease inhibitors, polymerase inhibitors, and assorted antiviral therapies. Also in development are a handful of potential therapeutic vaccines.²⁸

Researchers are also testing whether some medicines already on the market to treat unrelated conditions might be useful for people living with HCV. Most notably, some researchers and observers have been excited about nitazoxanide, a drug approved by the FDA in 2002 to treat two intestinal parasites. A small study indicated that the drug might help HCV-positive patients achieve SVR. Far more extensive studies are needed to verify this finding, however, and to identify possible side effects and longer-term impact.

While most of the drugs in the pipeline are currently undergoing Phase II trials or have not even reached that point, a few have already started Phase III trials.²⁹ Even so, it is not likely that a new anti-HCV drug from any class or category will be on the market for at least two years. Moreover, it is likely that most new drugs will need to be used in combination with either ribavirin or pegylated interferon (or both); therefore, the high-price obstacle is not likely to be overcome even with the introduction of one of the new compounds in development. Instead, it is likely that the overall cost of HCV treatment will increase when a new drug is added to a treatment regimen.

²⁸ A comprehensive discussion of HCV medicines being developed may be found in the Treatment Action Group's 2008 Pipeline Report, "HIV, tuberculosis, hepatitis B, and hepatitis C: Drugs, diagnostics, vaccines, and microbicides in development," released July 2008. Available online in PDF format: www.treatmentactiongroup.org/assets/0/16/42/196/198/a8611995-345d-487.

²⁹ Phase II and Phase III refer to different stages of clinical trials, which are undertaken to test the efficacy, effectiveness, and safety of an experimental drug or treatment. There are four phases in all. Depending on the product being tested, it can take years for all phases to conclude and the drug to be approved by, for example, the FDA. A majority of experimental drugs or treatments do not even get that far because their hoped-for benefits do not materialize during the clinical trials process. (According to the U.S. National Institutes of Health, "In Phase II trials, the experimental study drug or treatment is given to a larger group of people (100–300) to see if it is effective and to further evaluate its safety....In Phase III trials, the experimental study drug or treatment is given to large groups of people (1,000–3,000) to confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow the experimental drug or treatment to be used safely." See www.clinicaltrials.gov/ct2/info/understand.)

6. Issues Influencing Access to HCV Services

Not all, or probably even most, of the estimated 10 million people living with HCV in Eastern Europe and Central Asia have experienced severely debilitating or painful symptoms from their infections. The majority eventually will, however, unless they receive treatment. Access to treatment can literally be a matter of life or death: HCV-related liver diseases, from cirrhosis (which nearly one third of patients will eventually contract, if untreated) to liver cancer, are often fatal over time.

As summarized in Section 5, current HCV treatment options have significant limitations even in the world's wealthiest nations. The fact that the recommended treatment regimen effectively clears the virus in only half of patients is far from reassuring. But most people living with HCV are willing to accept those odds—and risk drug side effects to the fullest extent possible—if treatment and care are made available to them.

Far too few HCV-positive people in Eastern Europe and Central Asia ever get the chance to make that decision because comprehensive HCV treatment reaches only a small percentage of those who might want or benefit from it across the region. For one thing, most do not know they are infected or have not even heard of the disease. Secondly, as noted at the end of the HCV diagnostics discussion in Section 3, those who are aware of their status may find such knowledge to be of questionable value because they do not have access to HCV medicines of any kind.

6.1 HCV by the Numbers

Information about all HCV-related services is difficult to obtain across the region due to a combination of insufficient awareness, nonexistent political will, denial among health care providers and patients, inadequate surveillance systems, and conscious efforts to de-prioritize service delivery in the face of prohibitive costs of HCV medicines. With those caveats in mind, listed below are some key current estimates, factors and issues related to HCV care in the region:³⁰

³⁰ Unless specified otherwise, the data and observations in all of these bullet points are derived primarily from the following source: "Hepatitis C among injecting drug users in the new EU member states and neighboring countries: Situation, guidelines and recommendations," a report released in 2007 by the Eurasian Harm Reduction Network; online in PDF format: www.integration-projects.org/publications/hepc/Hep_C_report_info_for_distribution_2007_Final.pdf. This publication provides the most updated and comprehensive information on HCV treatment and care in the region, but it does not cover all 15 countries in the former Soviet Union. The 13 countries surveyed included the two most populous ex-Soviet states, Russia and Ukraine, as well as Belarus, Estonia, Latvia, and Lithuania. (The other seven countries are Bulgaria, the Czech Republic, Hungary, Poland, Romania, Slovakia, and Slovenia.)

- **12,600 Euros (\$16,000):** The per patient cost (averaged across countries) of a full course of HCV treatment involving ribavirin and pegylated interferon, the most highly effective recommended regimen. In Russia, the country in the region with the largest HCV burden, the cost is more than \$25,000.³¹
- **2:** Countries in the region that have successfully sought financial assistance from international entities to support HCV treatment—albeit on a limited basis so far and for HIV-positive people only. Belarus has allocated money from a Global Fund grant to treat up to 50 people, while Ukraine uses World Bank funds to support the provision of HCV treatment to a limited number of individuals. (Reports from the country indicate that nearly 250 patients were on treatment in Ukraine by the end of 2008.) Both projects began in 2007.
- **1:** Countries (Russia) in which only HIV-positive patients are currently eligible to receive free HCV treatment through the public sector. (This is not the only restriction, however. To be eligible, patients also must register at an AIDS center and subsequently be classified as “disabled.” Moreover, medicines to treat HCV infection are only provided free of charge to non-drug-using individuals.)
- **1:** Countries (Estonia) in which all costs of HCV treatment, including the recommended standard regimen, are covered by a state health insurance scheme.³²
- **o:** Countries in the region that have specific national documents that address hepatitis.
- **o:** Countries with HCV treatment guidelines that specifically recommend not excluding IDUs for treatment and, instead, call for treatment decisions to be made on a case-by-case basis.
- **o:** Countries in which all potentially useful HCV diagnostic tests—including HCV antibody tests, viral load tests, genotype tests, and liver biopsies—are available free of charge and without any restrictions.³³

³¹ Less effective regimens are much cheaper. A full course (48 weeks) of treatment with ribavirin and regular (i.e., non-pegylated) interferon costs about \$3,200 in Russia.

³² This scheme provides nearly universal coverage because more than 90 percent of Estonians are currently enrolled in it. However, the share is much lower among members of some marginalized groups—such as IDUs, of whom less than half are thought to be enrolled—who are most likely to need HCV treatment.

³³ According to the Eurasian Harm Reduction Network report, there is great variation across the region as to what kind of diagnostic tests are available and whether patients must pay for them. It is clear, though, that in no country are tests available free of charge to everyone who might want or need to be tested. The report notes the following, for example: “Confirmatory tests, RNA and genotype tests are reimbursed in most countries, except Ukraine. In Russia, antibody tests are free of charge for patients with health insurance, but they must pay for all other tests. In Lithuania diagnostic tests are purchased centrally by the state, therefore a limited number of people can undergo diagnostic tests each year.” The situation

Inconclusive though they may be on their own, taken together these numbers and data clearly indicate that access to comprehensive HCV treatment is insufficient nearly everywhere in the region. Obstacles exist no matter where people live. It is undeniably true that an HCV-positive individual is better off in the Baltic nations, where at least some form of treatment is generally available free of charge or at little cost, than in Ukraine (for example), where patients can expect no direct help from the state in terms of treatment.

Yet while important, these differences are marginal in terms of the overall picture. Regardless of whether the highest quality HCV treatment regimen is currently available to many patients, a handful of patients, or none at all, the regimen's current cost makes such treatment unsustainable at both a personal and society-wide level in all countries of the region. The majority of patients in need would never be able to pay for a full course on their own, even if they were not—as most currently are—among the poorest and most marginalized members of society. It is equally unrealistic to assume that governments in most of these countries could cover such costs themselves even if they ever committed to do so.

Therefore, the first step toward ensuring access to the most effective HCV treatment regimen for all individuals who want and need it is to increase awareness about all issues related to HCV, including the critical need for a comprehensive, strategic, and viable response. A detailed discussion of why and how to do that—and why civil society must be involved more extensively—is found in Section 7.

appears to be far worse in Central Asia, which was not covered by the report. In a September 2008 e-mail message, a health care advocate in Kyrgyzstan said that patients must pay up to \$100 for an HCV antibody test. She added that because testing supplies are often out of stock in Kyrgyzstan, some people have been forced to travel to Kazakhstan to be tested; that requires paying not only \$100 for a test in Almaty (Kazakhstan's largest city), but also travel costs of at least the same amount.

7. Looking to the Future: Building HCV-specific Civil Society Awareness and Advocacy

A handful of civil society groups in the region—notably the Eurasian Harm Reduction Network and its affiliated members—have focused specifically on HCV issues. For the most part, though, the local civil society response has been limited or nonexistent. HCV often seems to be viewed and presented as an afterthought concern even among organizations and advocates that seek to improve health care and access for IDUs. The number of NGOs in the region dedicated to HCV can be counted on one hand; in comparison, hundreds of such groups are working on HIV-related issues. Networks of HIV-positive individuals are driving demonstrable change in access to HIV treatment and society-wide awareness and stigma reduction. No such networks exist for or are driven by HCV-positive people.

The lack of civil society attention and voice is an important factor behind the low level of awareness about HCV across the region. Little change is likely in terms of treatment, care, or prevention unless this situation changes. Experience indicates that governments and most other public health stakeholders in the region will not act unless prodded and (in some contexts) shamed by advocates and patients.

All stakeholders must understand that inattention to HCV issues has already had serious individual and public health consequences that directly affect efforts to prevent and treat a host of other conditions, including HIV and drug dependence. The situation will only get worse if HCV does not receive the attention it deserves in the future. **This points to a top priority that should be considered the overarching recommendation of this paper: NGOs in the region should build their capacity to advocate around all issues related to HCV.**

The following steps could help boost the extent, quality, and effectiveness of civil society engagement:

- Existing HIV-oriented and harm reduction NGOs should allocate more and improved resources, both financial and human, to HCV. All personnel should understand specific issues related to HCV diagnostics, treatment, care, prevention, and risk factors. Dedicated advocates must have the capacity and support to engage in HCV advocacy efforts at local, national, and regional levels.
- Domestic and international civil society organizations should help establish and support viable networks of HCV-positive individuals. Such networks should be encouraged to collaborate with each other across local, national, and regional boundaries.

- Strategic thinking on HCV must be improved across all relevant sectors. To that end, all NGOs working on issues related to drug use, HIV, and harm reduction should collaborate to establish national and regional strategies around HCV. They would be joined in such initiatives by HCV-specific NGOs once such groups are established and viable.
- Civil society groups in the region can and should play a greater role in advocacy regarding patent and intellectual property issues in regards to medicines in general, and to HCV therapies in particular. They will likely need significant training in these areas in order to have the capacity and willingness to understand such complex issues and to help identify strategies to overcome trade- and patent-related barriers to drug access and affordability. Assistance and training would best be provided by international civil society groups that currently work on these issues around the world, including in the region.
- Patients and community-based groups in the region would benefit greatly from HCV treatment literacy and preparedness training and programs. Increased awareness and understanding among patients as to all issues related to HCV treatment would empower them by providing the skills and confidence they need to advocate more effectively on their own behalf. Targeted and enhanced treatment literacy could also play a major role in directly addressing many patients' common myths and fears about treatment.

Such efforts have been initiated extensively (and with great success) in tandem with HIV treatment expansion around the world, including in several countries of Eastern Europe and Central Asia. Existing HIV treatment literacy and preparedness training models—many of which are supported by international NGOs—could be adapted for HCV.

A preliminary effort toward achieving these long-term objectives has in fact been launched recently by the Eurasian Harm Reduction Network and OSI, two leading civil society organizations with expertise and interest in essential medicines issues. At a meeting in Kiev, Ukraine in March 2009, the organizations committed to help train local NGOs in HCV treatment and care, and assist the NGOs to advocate for increased access to services in their own countries and across the region. Among the key priorities will be capacity-building in intellectual property rights and international trade laws, complicated issues that greatly influence availability of affordable, effective HCV drugs and diagnostics.

Why and How ‘Generic’ Has Different Meanings

In regards to drugs, the term “generic” can have more than one meaning:

1. It refers to the chemical name of a drug, which remains the same regardless of the name used to market and sell the product by the manufacturer. For example, “ibuprofen” is the chemical name of a non-steroidal anti-inflammatory drug commonly used as a pain reliever. It is sold under literally hundreds of different names worldwide, including Brufen and Ipren (both available in Russia and other countries in Eastern Europe and Central Asia).
2. It refers to drugs that are chemically identical to brand-name drugs—i.e., those sold by companies that have or had exclusive patents to sell the drug in a given country, often because they developed the drug themselves. Generic drugs are nearly always cheaper than those produced, marketed, and sold by the “originator” company. With few extraordinary exceptions, most countries only allow the sale of generic drugs after patents have expired or if a drug has never been patented.

Most countries also do not permit a generic drug to be sold unless it has been certified by a reputable regulatory agency as meeting the same standards of safety, purity, and effectiveness as its non-generic counterpart. A generic medicine that has been approved by the World Health Organization or the U.S. Food and Drug Administration, for example, is generally considered to be of appropriately high quality.

Both of the two meanings above are relevant in this report, depending on the circumstance. “Ribavirin,” “interferon,” and “pegylated interferon” are chemical names of the three drugs used in HCV treatment.

However, in regards to the second definition above, generic versions of previously patented drugs are only available for ribavirin (in some, although not all, countries). The main reason that interferon and pegylated interferon are so much more expensive than ribavirin is precisely because no generic versions have been developed.

7.1 Potential Follow-up Priority: Generic Production of Pegylated Interferon

Increased civil society engagement and influence could help lay the groundwork for a radical and potentially useful approach to resolving the biggest obstacles to an effective HCV response. Although improved HCV prevention is certainly needed, of more immediate concern to governments, civil society and their domestic and international partners should be the initiating of efforts to expand access to treatment. In the absence of comprehensive, affordable, and effective treatment, there is little incentive for people to be tested for HCV. In such a situation, as has been shown over the years in regards to HIV, many individuals

prefer ignorance to being burdened with the knowledge that they have a potentially fatal condition for which there is no treatment. Prevention efforts, meanwhile, tend to be more effective when people know they are infected. That knowledge often prompts them to change behaviors that can put them and others at greater risk for poor health outcomes, such as sharing unsterilized injecting equipment and (especially for those living with HCV) heavy alcohol use.

Expanding access to treatment will not be easy. As discussed in Section 5 of this report, no new medicines to treat HCV are likely to be available anywhere in the world for several years. Therefore, an immediate focus of advocates, public health officials and policymakers worldwide—including those in Eastern Europe and Central Asia—should be on expanding access to the best option currently available: dual therapy involving ribavirin and pegylated interferon.

Expanded access in any meaningful way is not feasible in the current environment, however, given the high prices charged by the two makers of pegylated interferon. Affordability is only likely to be achieved through one (or preferably both) of the following strategies: i) negotiating with the two brand-name companies to lower their prices, perhaps in exchange for a guaranteed purchase amount over time, and ii) getting generic products onto the market. It is highly probable that the first strategy would only be successful if the second one were under way in a serious, sustainable manner.

To date, though, few steps—and none successful—have been taken anywhere in the world to develop generic pegylated interferon products. One reason stems from the complex nature of interferon. It is a biologic, not a conventional small-molecule drug, and is thus relatively difficult and expensive to manufacture. There are also significant regulatory consequences to being a biologic in much of the world. In the United States, for example, generic authorization for biologics is not currently available (although activists are working to overcome that restriction). The result, as summarized recently in the *New York Times*, is that “because there is no established regulatory pathway for approval of generic versions of biologics, companies that make large-molecule drugs [biologics] have been able to charge monopoly prices.”³⁴

Such obstacles are not insurmountable, as evidenced by the ultimately successful effort to facilitate the making and distribution of low-cost, generic HIV drugs in several different countries. Advocates and public health policymakers should keep in mind the potential payoff in terms of lives improved and saved: a viable generic or two could cause a major revolution in HCV treatment.

³⁴ Natasha Singer, “In Wyeth, Pfizer sees a drug pipeline,” *New York Times*, January 27, 2009.

Domestic production of safe, reliable, and effective pegylated interferon would not be easy even in Russia or Ukraine, the two best-positioned countries in the region in which generic versions could conceivably be developed. Yet it might be quicker than waiting for new medicines to come on the market—and even then it is likely that those drugs, also brand-name, would be equally unaffordable, if not more so. Once produced in the region, generic pegylated interferon could be made available elsewhere in the former Soviet Union.

Some lingering concerns remain about the quality of pharmaceutical products made in Russia, Ukraine, and other countries in Eastern Europe and Central Asia. Sufficient capacity and expertise may nevertheless be available to overcome the poor quality perception, especially if adequate incentives are provided and oversight improved. Russia, for example, currently has some 300 pharmaceutical companies. Most are relatively small and make only a handful of unsophisticated products. A few, though, may have the scope and scale to produce generic versions of products considered biologically complex. One publication noted the following, for example:³⁵

Russia is a country which has a long biotechnology tradition and a high level of expertise in the relevant disciplines. Furthermore, labor costs for such R&D experts are surprisingly low. Therefore, Russian biotechnology institutes or companies may have the potential to expand in order to deal with manufacturing generic biologics in a way that proves competitive in Western Europe and the US. However, this means that they must first overcome financial difficulties in terms of funding.

Advocates in the region should also recognize, however, that potential does not always lead to efficient or timely action. Relatively limited generic drug production experience and regulatory obstacles in the region mean that a more feasible and cost-effective initial approach might be to focus on importing generic pegylated interferon from other countries. This would require working with health care activists and policy experts from outside the region to identify the most promising countries and companies. A long-term goal of global sourcing HCV medicines from India or China, for example, could be easily justified in light of the innovation exhibited by many Indian and Chinese generic manufacturers and their governments' history of resisting patent-related pressure from brand-name firms.

³⁵ "Considerations about generic biologics," a 2004 report from a researcher affiliated with TechNova Medical Products. Available online in PDF format at www.sicor.lt/bin/ACFB481.pdf.

8. Specific Recommendations

Despite its scope and increasingly dire public health consequences, HCV remains a largely silent and hidden epidemic across Eastern Europe and Central Asia. A recent report on HCV and harm reduction concluded the following: “In...much of Asia and Eastern Europe, the response to HCV is nascent and governments and civil society alike are just beginning to form a response to growing epidemics.”³⁶ That conclusion does, however, contain a kernel of good news—about “beginning to form a response”—that is likely to be the cornerstone of both short- and long-term efforts to improve the health of people living with HCV.

This section seeks to jumpstart that response. It contains a series of recommendations intended to expand and improve access to HCV services across the region. All support the top priority discussed in Section 7: the need to build HCV-specific civil society awareness and advocacy in the region. They should be considered complementary recommendations to be acted upon simultaneously.

1. Recommendations Regarding HCV Surveillance, Awareness, and Testing

- **Government agencies and civil society should collaborate in devising, implementing, and monitoring the effectiveness of expanded efforts to gather data and surveillance on HCV prevalence and trends.** It is extremely difficult to combat an epidemic in the absence of reliable data on transmission trends and prevalence. Prevention programs are much more effective when they can be targeted to regions, communities and individuals most in need or most at risk. The same holds true for treatment programs. Health care budgets at all levels are far more realistic when policymakers can more accurately predict treatment needs over time.

Some countries have made better efforts than others (notably the Baltic states), but adequate and reliable information on the HCV epidemic is missing throughout the region. Devising and implementing better surveillance systems is a critical early step toward ensuring that all people in need receive access to HCV treatment once it becomes more widely available.

³⁶ See “Global state of harm reduction 2008: Mapping the response to global HIV and hepatitis C epidemics,” published in 2008 by the International Harm Reduction Association. Available online in PDF format: www.ihra.net/Assets/582/1/GSHRFULLReport.pdf.

Civil society groups and advocates should recognize that government officials often justify their lack of action on treatment to a lack of adequate data. That is a poor excuse that should not go unchallenged. Advocates should seek to hold government officials accountable to improving HCV prevention and treatment efforts at the same time that they expand data collection. They need not, and should not, wait to provide better quality HCV care until better data and surveillance systems are in place.

- **Government agencies and civil society should collaborate in devising, implementing, and monitoring the success of extensive HCV awareness campaigns.** Broad-scale campaigns for the general population should be accompanied by much more intensive, focused campaigns aimed primarily at members of vulnerable groups, such as IDUs—which is a key reason that civil society must be involved at all stages. The campaigns should start with the basics: what is HCV, what are the risk behaviors, how and where can people be tested, etc.

Campaigns must also target individuals living with HCV. Greater knowledge and support may increase their ability and inclination to i) avoid potentially risky behaviors that could transmit the virus to others, and ii) take other health promotion measures, such as reducing alcohol intake, that can help ease stress on their livers. Civil society would play a crucial role in such efforts because IDUs and members of other vulnerable groups often distrust or fear government entities based on real or perceived instances of discrimination and harassment.

- **All health care facilities should provide HCV diagnostics free of charge to all who want or need a test.** Expanded awareness campaigns of the type discussed in the previous recommendation are useless unless HCV antibody tests (at the very least) are widely available. All individuals should be able to obtain a test, confidentially if requested, at all public-sector health facilities. Testing should be accompanied by standardized pre- and post-test counseling provided by specially trained personnel. Such counseling need not be onerous and time-consuming as long as accurate, basic information is provided as well as referrals to health and social services if necessary.

Confirmatory tests, such as PCR tests, should also be available to those whose HCV antibody tests come back positive. If facilities do not have the materials and expertise to administer such tests themselves, they should assist the patient in obtaining free tests at another site. The same conditions should apply to other tests of importance to HCV-positive individuals, including genotype tests.

Personnel at testing facilities should also be prepared to assist patients in obtaining care should they test positive for HCV. Many will not need or want medical treatment, but they must have access to caregivers who can help them make fully informed decisions over time. Health care personnel should also be prepared to discuss and outline the benefits of testing in the absence of viable treatment options. Patients are often reluctant to take on the anxiety related to a confirmed diagnosis if there is little that can be done to help them.

2. Recommendations to Expand Access to Affordable HCV Treatment

- **Government officials and domestic pharmaceutical companies in the two most populous nations in the region—Russia and Ukraine—should collaborate to consider the possibility of developing, supporting, and sustaining the production of safe and effective generic versions of pegylated interferon.** Even if fully or partially state-owned, as is often the case in the former Soviet Union, domestic pharmaceutical companies currently have little incentive to undertake development and production of pegylated interferon—which is, in any case, a complex process. Thus the initiative must be structured, at least initially, as a partnership involving relevant government agencies. Health officials are obviously necessary, but so too are trade and patent officials, who will need to take the lead in negotiating with one or both of the multinational companies (Roche and Schering-Plough) currently making and selling patented pegylated interferon compounds. It is possible that the companies would issue licenses allowing the local production and distribution of low-cost pegylated interferon in return for retaining a formal patent. Such a step has been undertaken successfully in at least one country (Egypt) already, as discussed in Box G.
- **Civil society advocates and government officials in Eastern Europe and Central Asia should explore the possibility of global sourcing from outside the region.** There are many benefits to focusing on manufacturing generic HCV medicines in the region, including the long-term improvement in technical capacity. However, as discussed in Section 7, economies of scale are important in regards to drug production, especially for biologics such as pegylated interferon, and companies in countries such as India and China may be better placed to develop and ramp up production more quickly and cheaply. There are benefits from the perspective of intellectual property and patents as well. As even most Russian and Ukrainian officials would acknowledge, those countries' governments are also more likely to

take seriously a compulsory licensing request for domestic manufacture of generic pegylated interferon.

- **Government officials and policymakers in the region should exercise far greater political will and commitment to override patents and take other similar measures to make much-needed medicines more affordable on the domestic market, especially for public health systems.** This recommendation is closely related to the two immediately preceding ones. It has a broader aim, however, because it applies not just to HCV medicines but to all essential medicines.

Russia and other countries in the former Soviet Union have been notoriously reluctant to consider policies and measures to lower health care outlays by prioritizing the purchase and distribution of generic medicines, even when such drugs are widely (and safely) used elsewhere. This is one reason why, for example, lower-priced, generic HIV drugs have yet to be purchased and distributed even as tens of thousands of people start taking ART every year through the Russian government's HIV treatment program. Because it refuses to purchase generics, the government's per-patient cost is much higher than many other countries with comparably sized economies (such as Brazil). The overall cost of its HIV treatment expansion efforts will skyrocket even further when it assumes responsibility for treating HIV patients currently receiving care through the Global Fund.

The same problem will occur with HCV treatment if policymakers refuse to consider new strategies—especially the introduction of generic competition—so they can afford important life-saving drugs for the majority of HCV-positive individuals who need them.

A major obstacle has been longstanding assumptions among Russian officials and many domestic patient advocates that generic medicines are by nature inferior to brand-name drugs. That may have once been true in the region, but it need not be if adequate monitoring and safeguards are put in place. Plenty of evidence is available showing that generic drugs for most conditions, including HIV, are safe and effective.

If Russian officials are not confident that local companies can produce safe, effective and reliable generic medicines, then now is the time to invite WHO officials to help implement new standards, practices, and policies. There seems to be little to gain by resisting change that could greatly reduce health care costs and increase access to medicines for people in need.

- **Government officials—ideally from health care agencies—from across the region should establish a formal working group to facilitate inter-regional cooperation in improving access to HCV treatment. At least one civil society representative from each country should participate as well.** Although scope and scale differ somewhat, all countries in the region have growing HCV epidemics and are unable or unwilling to provide HCV treatment to more than a fraction of those in need. Migration among most of the countries is also common, especially in regards to laborers from Central Asia working seasonally or for extended periods of time in Russia. These are just a few of the reasons that a collaborative response to HCV is likely to be more effective for all involved than a series of individual ones. Governments might, for example, harmonize and link surveillance systems and agree to share technical expertise and financial resources.

Inter-regional cooperation is also important in regards to ramping up HCV treatment in the event that lower-cost generic medicines become available in the region. A working group involving health care officials from across the region can facilitate this process by creating one treatment standard and arranging contracts and agreements that ensure efficient and timely distribution and procurement. The working group could also establish a transparent dispute resolution mechanism through which advocates, health care personnel, and patients could raise concerns regarding HCV treatment availability and access.

- **Health care officials and medical personnel should commit to providing only the highest quality HCV treatment: combination therapy with ribavirin and pegylated interferon.** In many countries in the region, all or the majority of patients lucky enough to receive HCV care are provided with substandard treatments in terms of effectiveness. Such treatments generally consist of combination therapy with ribavirin and non-pegylated interferon, or simply interferon monotherapy, or inadequate side effects management.

In the long run, substandard treatment is not cost effective given the health-related consequences that can occur from untreated or inadequately treated HCV infection. HCV can be a debilitating and deadly disease; patients deserve the best treatment available. Health care officials should start making plans now to ensure that all in need receive high quality medicines as soon as the lower-priced versions are available.

- **Health care officials, civil society partners, and patient advocacy groups should explore in greater detail the possibility of using Global Fund programs to pay for HCV diagnostic and treatment services.** As noted in Section 6, this would

not be unprecedented in the region: Belarus has allocated Global Fund money to cover the costs of HCV treatment for a small number of patients. Such efforts could perhaps be implemented elsewhere if the case can be made, for example, that the provision of comprehensive HCV services would complement and enhance HIV- and TB-related services provided to IDUs in particular.

Pilot projects could be an initial step. For existing grants, national Global Fund country coordinating mechanisms (CCMs) could seek permission to utilize already allocated or promised funds to provide HCV services. CCMs could also explicitly include such projects, and their rationalization for doing so, in future Global Fund applications as well.

3. Recommendation to Guarantee Equity in HCV Services Access

- **IDUs must be guaranteed equal and full access to all HCV-related services, including treatment.** Discrimination against IDUs is not only inhumane and unfair, but also incredibly short-sighted from a public health perspective. IDUs comprise a disproportionate share of HCV-positive individuals in all countries of Eastern Europe and Central Asia. The epidemic has no chance of being addressed effectively if IDUs are unable or unwilling to obtain comprehensive care, including medicines that could conceivably clear the virus from their systems.

Box G.

Potential Role Model: Production of Pegylated Interferon in Egypt

Generic versions of ribavirin have been available in much of the world for the past few years. Most appear to be safe and work effectively; in Russia, for example, a recent report concluded that “new Russian oral ribavirin-containing agents” proved to be “bioequivalent”³⁷ when compared with the “original agent Rebetol.”³⁸ (This observation is important because it shows that companies in Eastern Europe and Central Asia have the ability and capacity to make safe and effective generic medicines, including at least some of those used to treat HCV.)

There are, however, no generic versions of the other drug in the HCV standard of care combination treatment regimen: pegylated interferon. Two companies currently control the pegylated interferon market through their branded, patented products. Both Roche, which makes Pegasys, and Schering-Plough, which makes PegIntron, have little incentive to provide proprietary information to help speed up the development of these complicated compounds. That is one reason that researchers in parts of the world who reportedly are seeking to develop generic versions of pegylated interferon are thought to be years away from achieving success.

The situation is not entirely dire, however. There has been at least one noteworthy and interesting development in regard to producing and distributing lower-priced pegylated interferon. Since 2006, an Egyptian pharmaceutical company, Minapharm, has been selling an HCV drug for the domestic market called Reiferon Retard, which reportedly is bioequivalent to Pegasys. The initial price of Reiferon Retard was one quarter that of the two brand-name drugs, a price differential that enabled the new drug to quickly take a significant market share—over half that of the private market by early 2009, according to the company. Both Roche and Schering Plough have lowered the prices of their drugs in response to the competition. Such developments are extremely important in Egypt, given that perhaps one-fifth of the population is living with HIV (see Box B).

Technically speaking, Reiferon Retard is not really a “generic” drug. The Egyptian company is able to produce and sell its version legally because it secured a license on the drug’s manufacturing process—from a German biotechnology company—before new global trade laws greatly strengthened patent protection a few years ago. It has not attempted to sell its version outside of Egypt, and would very likely be unable to do so because of current patent restrictions.

The example is nevertheless instructive for Eastern Europe and Central Asia because it indicates that key biological information for creating a viable version of pegylated interferon could perhaps be obtained with some persistent effort. Companies such as the German one that supplied information to Minapharm could be approached and asked to provide similar resources to help domestic pharmaceutical companies in Russia and Ukraine, for example, develop similar products.

³⁷ The term “bioequivalent” means that the medicines have been studied and found to be safe and to work equally effectively. There is no difference between a brand-name drug and a generic version that is “bioequivalent” to it—except, most likely, the price. Generic medicines are nearly always much less expensive.

³⁸ See www.find-health-articles.com/rec_pub_18942422-comparative-estimation-pharmacokinetics-generic-ribavirin-containing.htm.

Shining a Light on a Hidden Epidemic

Hepatitis C presents a serious health threat worldwide. Some 150 million individuals are currently living with the virus and three to four million people become infected every year. Hepatitis C's impact is particularly devastating in Eastern Europe and Central Asia, where infection is strongly correlated with injection drug use. Yet, the cost of treatment remains prohibitive to most people in the region. Lack of effective treatment not only causes serious harm to individuals, it directly impacts the ability of countries to respond to the growing HIV epidemic. The situation will only get worse if health authorities and policymakers do not take action to shine a light on this hidden epidemic.

