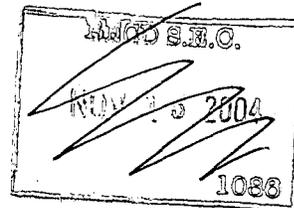
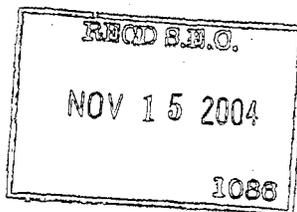


# Media Release



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## Pegasys receives new indication in Europe allowing hepatitis C patients with "normal" liver enzyme levels to be treated

### A large number of hepatitis C patients gain access to therapy

Roche announced today that the European Medicines Agency (EMA) has approved Pegasys for the treatment of hepatitis C patients with persistently "normal" liver enzymes. This extension of the current label is based on the results of a pioneering study<sup>1</sup> that showed that combination therapy with Pegasys eradicated the virus (sustained virological response) in more than half of this patient group. Under current treatment guidelines, hepatitis C patients with normal liver enzymes would not normally be eligible for treatment.

As a result of this breakthrough study, the EMA has recognized that patients who have 'normal' alanine aminotransferase (ALT) levels should be assessed for treatment in the same way as other chronic hepatitis C patients and that normal ALT status *per se* should no longer be considered a barrier to treatment. Pegasys is the only pegylated interferon that has an indication in the EU for these patients, who account for approximately 30% of the total hepatitis C patient population.<sup>2</sup>

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#### 'Normal' ALT patients traditionally untreated

Measuring ALT is the most common method used by physicians to try to assess whether a hepatitis C patient has ongoing liver damage<sup>3</sup>. When liver cells are damaged, ALT is released into the bloodstream. If a patient had a 'normal' amount of ALT, they were considered to have mild disease and not in need of treatment, and often referred to as 'healthy carriers'. In fact, it was thought that treating these patients could potentially worsen their disease.<sup>4</sup>

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It has become apparent, however, that having 'normal' levels of ALT does not necessarily mean that the liver is undamaged; studies have shown that about 80% of these patients have some degree of liver damage and one third have significant liver damage<sup>5</sup>. Unfortunately, since these patients were routinely excluded from treatment, they were not included in clinical trials assessing

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the safety and efficacy of new pegylated interferons and therefore the risk:benefit of treatment remained unclear – until now.

“By removing the stipulation that patients must have elevated levels of this biochemical marker before being considered for treatment, the EMEA is facilitating a positive change in how physicians make decisions and offering more patients to a chance of a cure,” said Professor Stefan Zeuzem, Director of the Department of Internal Medicine at the University Hospital in Homburg, Germany, and the lead investigator of the study on which the approval was based. “It marks a new era in our understanding of how best to treat patients and underscores that the decision to treat should be based on multiple factors rather than simply on ALT.”

#### **Revised Pegasys labelling information**

In 2002, the EMEA approved Pegasys for the treatment of chronic hepatitis C in adult patients with *elevated* transaminases and who are positive for serum HCV-RNA, including patients with compensated cirrhosis. In the EU, this criterion for elevated ALT has now been removed only from the Pegasys label, marking another distinction for this compound.

#### **The research that informed the EMEA decision**

The approval was based on the first and only large, randomized, multinational study examining the benefit of treatment in this underserved patient population. The study involved 514 patients that were randomized into one of three arms: one arm included patients selected to continue with observation but no treatment, since this approach was considered the current standard of care at that time. The other two arms randomized patients to treatment with Pegasys (180 mcg/weekly) and Copegus (800 mg/daily) for either 24 or 48 weeks.

The following summarizes the research findings:

- Nearly 30% of patients of patients were found to have some degree of liver scarring (fibrosis) and/or evidence of hepatic inflammation, despite a ‘normal’ ALT reading.
- Overall, 52% of the treated patients achieved a sustained virological response (SVR – or cure) while no patient spontaneously eradicated their virus in the untreated group.
- Consistent with findings from studies involving patients with elevated ALT levels<sup>6</sup>, 72% of patients infected with genotype 2 or 3 treated with Pegasys combination therapy achieved an SVR after just 24 weeks of treatment and 40% of difficult-to-treat genotype 1 patients achieved an SVR after 48 weeks of therapy.
- The incidence of the most common interferon-related side effects was lower than in previous studies with this population and similar to those seen in HCV patients with elevated ALT levels treated with Pegasys combination therapy

"The question of whether or not persistently 'normal' ALT patients should be treated has been a long-standing issue in the hepatitis C community," said William M. Burns, Head of Roche's Pharmaceutical Division. "As a company, we are proud to bring this issue to resolution and delighted that Pegasys combination therapy is the treatment that will be of benefit to these patients."

#### **About Pegasys**

Pegasys, the market leader worldwide in hepatitis C therapy, provides significant benefit over conventional combination interferon therapy in HCV patients of all genotypes. The benefits of Pegasys are derived from its large 40 kilodalton (KD) branched-chain polyethylene glycol (PEG) construction, which allows for sustained drug levels over the course of a full week. Pegasys also distributes more readily to the liver (the primary site of infection) than conventional interferon. Pegasys is the only pegylated interferon available as a ready-to-administer solution. Each weekly subcutaneous injection contains 180mcg of pegylated interferon alfa-2a (40KD), which is the approved dose for all patients, regardless of body weight.

#### **Roche in hepatitis**

Roche is committed to the viral hepatitis disease area, having introduced Roferon-A for hepatitis B and C, followed by Pegasys in hepatitis C and a full development program in hepatitis B. Roche has its own brand of ribavirin, Copegus, which is used in conjunction with Roferon A or Pegasys for HCV. In addition, Roche manufactures HBV and HCV diagnostic and monitoring systems: The COBAS AMPLICOR Test, and the AMPLICOR MONITOR Test, two testing systems used to detect the presence of, and quantity of, HBV DNA or HCV RNA in a person's blood. Roche has filed a new indication for Pegasys and Copegus as a treatment for patients co-infected with HIV-HCV and for Pegasys as a treatment for chronic hepatitis B. More than 40,000 patients worldwide continue to participate in trials with Pegasys and Copegus as Roche examines the unmet medical needs of hepatitis C patients. Roche's commitment to viral hepatitis also extends to its pursuit of strategic alliances and partnerships to develop new compounds for the future.

#### **About Roche**

Headquartered in Basel, Switzerland, Roche is one of the world's leading research-intensive healthcare groups. Its core businesses are pharmaceuticals and diagnostics. As a supplier of innovative products and services for the prevention, diagnosis and treatment of disease, the Group contributes on a broad range of fronts to improving people's health and quality of life. Roche is number one in the global diagnostics market, the leading supplier of pharmaceuticals for cancer and transplantation and a market leader in virology. In 2003 the Pharmaceuticals Division

generated 19.8 billion Swiss francs in prescription drug sales, while the Diagnostics Division posted sales of 7.4 billion Swiss francs. Roche employs roughly 65,000 people in 150 countries and has R&D agreements and strategic alliances with numerous partners, including majority ownership interests in Genentech and Chugai.

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**Further information:**

About Hepatitis C: [http://www.health-kiosk.ch/start\\_hepa](http://www.health-kiosk.ch/start_hepa)

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<sup>1</sup> Zeuzem, S. et al. International, multicentre, randomized controlled study for the treatment of patients with chronic hepatitis C and persistently normal ALT levels with peginterferon alfa2a and ribavirin. AASLD 2003 Boston.

<sup>2</sup> Conry-Cantilena C. et al. "Routes of infection, viremia, and liver disease in blood donors found to have hepatitis C virus infection. N Engl J Med. 1996;334(26):1691-6

<sup>3</sup> Kaplan MM. Alanine aminotransferase levels: what's normal? Ann Intern Med 2002;137(1):346-355.

<sup>4</sup> NIH. NIH Consensus Statement. Management of hepatitis C. National Institutes of Health. 1997

<sup>5</sup> Puoti, C. et al. Histological and virological features and follow up of hepatitis C virus carriers with normal aminotransferase levels: The Italian prospective study of the asymptomatic C carriers (ISACC). J Hepatol 2002;37(1):117-23

<sup>6</sup> Hadziyannis, S.J. "Peginterferon-alfa2a and Ribavirin Combination Therapy in Chronic Hepatitis C: A Randomized Study of Treatment Duration and Ribavirin Dose" Ann Intern Med. 2004;140:346-355.