I-MAK initiative for medicines access & knowledge

PATENT LANDSCAPE REPORT FOR PEGYLATED INTERFERON ALFA 2A & 2B

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1. BACKGROUND

It is estimated that around 170-200 million individuals around the world are currently living with the hepatitis C virus (HCV), with an additional 3-4 million becoming infected every year. Therefore, the overall incidence of HCV amounts to 3.3 % of the world population.[1] Statistically, this means as many people are infected with HCV as with HIV.

Egypt has the highest HCV prevalence rates, with an estimated 18% of the population infected. Other regions with high prevalence include Africa (in particular Burundi, Cameroon and Guinea), Eastern Europe (in particular Russia and Ukraine), Central Asia (for example, Georgia, Kyrgyzstan, Mongolia), South East Asia (Philippines, Thailand and Viet Nam) and South America (Bolivia and Brazil).

This makes HCV one of the greatest public health threats this century and possibly one of the greatest threats to be faced in the next. Indeed, without rapid intervention to contain the spread of the disease and to make treatments available and accessible, it is believed that the death rate from HCV will surpass that of AIDS by the turn of the century.[2]

1.2. Barriers to Treatment Access

There are a number of issues that serve to limit the response to HCV worldwide. These range from: the lack of surveillance data and time it takes for HCV to be detected; the stigma attached to treating injecting drug users (which make up a significant number of HCV patients); a lack of advocacy and awareness as compared to HIV; a lack of new and improved treatments; and the prohibitive costs for accessing the current recommended standard HCV treatment.[3] [4]

The current standard treatment for HCV consists of two medicines taken in combination, ribavirin and pegylated (PEG) interferon. While generic versions of ribavirin are available, access to the two current PEG interferon products, Pegasys (pegylated interferon alfa-2a) marketed by Genentech (now Hoffmann-La Roche) and PegIntron (pegylated interferon alfa-2b) marketed by Schering Plough (now

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[1] Hepatitis C, An Epidemic for Everyone, The C. Everett Koop Institute, http://www.epidemic.org/thefacts/theEpidemic/worldPrevalence/

[2] It is estimated that there are 350,000 deaths each year worldwide due to HCV. (Viral Hepatitis Prevention Board), *Viral Hepatitis*, Vol 19, No.1, January 2011.

[3] Hoover. J, *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*, Open Society Institute Public Health Program, August 2009.

[4] A number of investigational compounds that are all-oral and interferon-free are in Phases II and III of clinical trials, but are not expected to come to market until at least 2014/15. See Treatment Action Group, *2012 Pipeline Report HIV, Hepatitis C Virus (HCV) and Tuberculosis (TB) Drugs, Diagnostics, Vaccines and Preventative Technologies in Development*, (2012)

Merck) is understood to be restricted due to exclusive patent rights and/or regulatory hurdles that face biosimilar versions coming to market.

As patents can confer an exclusive right to manufacture and sell a product (including exporting and importing a product where a patent right exists), patent holders often demand a price for a medicine according to that which the market can bear. Without access to biosimilar PEG interferon products from competitors, a standard 48-week course of treatment for treating HCV can cost more than $20,000 in many resource-constrained countries.[5] As a result, government health systems are either unable or unwilling to pay such prices.

Companies that are able to manufacture and supply PEG interferon at a significantly lower price than PegIntron and Pegasys have been identified.

The Indian manufacturer Virchow Biotech Private Limited has developed a PEG interferon alfa-2b product that is currently marketed in India and claims to be a biosimilar version to Schering's PegIntron.[6] As the patent landscape report shows, Schering has filed an infringement action against Virchow based on its patents in India. Virchow has counterclaimed with a revocation action, claiming that Schering's patents are invalid. The matter is still in progress with a decision expected some time this year. Virchow is currently seeking regulatory approval for its product in a number of countries, including Brazil, Russia, Ukraine and Viet Nam.

Another available product is Reinferon Retard (pegylated interferon alfa 2a), which is produced and marketed in Egypt by the Egyptian company Minapharm Pharmaceuticals. However, it is understood that Reinferon Retard is not considered to be a biosimilar version to Roche's Pegasys given that the molecular weight of the product is outside the range claimed in the relevant patent.[7]

[5] Unlike ribavirin, which is a small molecule from the nucleoside analogue class, interferon is a biological product. As such 'generic' versions of biologic products are called biosimilars.

[6] This is based on Virchow's conjugated product having the same molecular weight and excipient as used in PegIntron. Further data is being sought to assess the profile of Virchow's product.

[7] Discussion at The Treatment Action Group, Open Society Foundations and Medecins Sans Frontieres meeting *Hepatitis : Building Consensus on the Way Forward to Increase Access to Treatment in Low-and-Middle Income Countries*, Paris, 25/26 September 2012.

2. THE PATENT LANDSCAPE

This patent landscape was prepared in order to determine where patent barriers might exist to the legal production, exportation or importation of biosimilar versions of the currently marketed PEG interferon products Pegasys (Hoffmann-La Roche) and PegIntron (Schering-Plough).

The landscape identifies patents covering interferon technologies that have been filed by or granted to Roche and Schering (including related companies e.g. Genentech and Merck), or patents licensed from another company (e.g. Enzon Inc.) to Roche and Schering. Out of the patents identified in the landscape, this report highlights the key ones that would likely be used to block biosimilar versions of Pegasys and PegIntron.

Patents filed or granted in Europe, the U.S or through the international patent system (PCT) were first identified. Using the European, US and PCT patent information, additional searches were then conducted to locate whether equivalent/corresponding patents had been filed or granted in countries specifically selected for this report: Brazil, Egypt, Georgia, Kyrgyzstan, India, Indonesia, Russia, Thailand and Ukraine. As the methodology below explains, some of the data for a selection of the countries was not available due to the absence of a searchable national electronic database or a lack of information.

This following section summarises the key patents that would likely pose a barrier to biosimilar production of the products Pegasys and PegIntron. The complete landscape and information is available in **Annex I**.

3. SUMMARY OF THE PATENT LANDSCAPE

Based on the patent information obtained, Roche's Pegasys product is protected in more of the territories covered for this report than Schering's PegIntron. Should Virchow successfully overcome Schering's patents in India and any regulatory barriers in importing countries, it should be able to export its version of PEG interferon alfa-2b to Brazil, Georgia, Kyrgyz Republic, Russia and the Ukraine.

3.1 Hoffman-La Roche/Pegasys

Product Background

Pegasys (PEG interferon alfa-2a) is a covalent conjugate of recombinant alfa-2a. The polyethylene glycol (PEG) polymer used in the Pegasys product is described as a bis-monomethoxy PEG and is present in a ratio of 1:1 with the protein molecule. The conjugated product has an average molecular weight of 60,000 daltons, of which the protein's molecular weight is approximately 20,000 daltons.

Key Patents

Ten patents in the name of Roche that claim a form of PEG interferon alfa were identified. The following patents are considered key for protecting the product Pegasys.

Interferon Conjugates

This patent covers the PEG interferon as used in the Pegasys product. Of all the key patents identified, this patent provides the strongest protection for Pegasys.

European/US/Pct Patent Nos.	Expected Expiry	Description/Claims based on EP/PCT Patents	Country Status
EP0809996 (Granted) US5382657 (Granted) No PCT application filed	22.5.2017	The claims cover a physiologically active PEG interferon alfa conjugate wherein the average molecular weight of the PEG units in the said conjugate is from 26,000-66,000 daltons. Also covered are pharmaceutical compositions.	Brazil – Granted Egypt – Granted Georgia – Granted Kyrgyz Republic – Granted India – Granted but revoked following appeal of post grant opposition Indonesia – NA Russia – Granted Thailand – NA Ukraine – Granted

According to information available, equivalent patents have been granted in Brazil, Egypt, Georgia, Kyrgyz Republic, Russia and Ukraine. The claims as granted in Georgia, Russia and Ukraine are equivalent to the claims as granted for EP0809996. The claims as granted in Brazil and Egypt were not available for this report. Although initially granted in India, the patent was recently revoked there following the appeal of a post grant opposition.

In order to avoid infringing this patent, and assuming the scope of the granted claims are identical to those in the European patent, biosimilar producers would have to ensure that the PEG fraction of their product does not fall within the molecular weight ranges claimed by Roche.

Interferon Solution

This patent is relevant as it covers the current formulation for the marketed product Pegasys. The scope of this patent is limited to the particular excipients used to formulate the PEG interferon used for Pegasys. Biosimilar producers would have to find an alternative formulation that does not correspond to the ingredients used in this patent.

European/US/Pct Patent Nos.	Expected Expiry	Description/Claims based on EP/PCT Patents	Country Status
EP0736303 (Granted) US5762923 (Granted) No PCT application filed	30.3.2016	This patent describes an aqueous solution of interferon alpha (preferably PEG interferon alfa-2A), which is suitable for parenteral administration. This formulation corresponds to the excipients listed in the summary of product characteristics (SmPC) for Pegasys.	Brazil – Suspended pending response to examination Egypt – NA Georgia – No patent found Kyrgyz Republic – No patent found India – Granted Indonesia – NA Russia – Granted Thailand – NA Ukraine – No patent found

According to information available, the equivalent patent is granted in Russia (although the claims require translation to assess their scope) and is suspended in Brazil pending Roche's response to the examination report. The searches did not reveal an equivalent patent in Georgia, India, Kyrgyz Republic or Ukraine.

Use of PEG interferon alfa and ribavirin

This patent provides protection for the use of Pegasys in combination with ribavirin. The scope of this patent is limited to the use of a particular dosage form of Pegasys with ribavirin.

European/US/Pct Patent Nos.	Expected Expiry	Description/Claims based on EP/PCT Patents	Country Status
PCT/EP99/03746 (WO99/64016) EP1087778 (Granted) US20030053986 US20050031589 US20070196385 (Abandoned)	29.5.2019	The main claim covers the use of PEG interferon alfa in association with ribavirin for the manufacture of a medicament for the treatment of chronic hepatitis C. Claim 4 claims the use wherein the PEG interferon alfa conjugate is PEG interferon alfa-2A as patented in EP 0809996 (Roche's key patent for PEG interferon alfa).	Brazil – Application refused, appeal filed Egypt – NA Georgia – No patent found Kyrgyz Republic – No patent found India – Granted Indonesia – Application filed (current status not available) Russia – Granted Thailand – NA Ukraine – No patent found

Equivalent patents were granted in India and Russia. The application in Brazil was refused, but is currently under appeal.

The three claims as granted in India cover a composition for the treatment of chronic hepatitis C comprising peginterferon alfa-2a with ribavirin. The composition provides that the peginterferon alfa-2a is 33 to 540mcg per week with 400 to 1200 mg of ribavirin daily.

The claims granted in Russia are the same as granted in the equivalent European patent EP 1087778.

No equivalent patents were found in Georgia, Kyrgyz Republic or the Ukraine.

With respect to Indonesia, the current information regarding the status of the application is not available.

Pharmaceutical formulation for interferons

The following patent is of interest because it claims an improved formulation over the one currently used for Pegasys (see European patent 0736303).

European/US/Pct Patent Nos.	Expected Expiry	Description/Claims based on EP/PCT Patents	Country Status
PCT/EP2008/ 004165 (WO08/145323)	25.5.2028	The key claims cover a pharmaceutical formulation comprising an IFN-α (including a PEG IFN-α conjugate) as active agent and an anti-oxidant for treating hepatitis C. This patent claims to be an improved formulation over the one currently used for Pegasys (see EP0736303 above).	PCT national phase data for the application is either not available or Roche has elected to not pursue the application in the territories of concern.

While this patent may not currently cover a marketed product, it is possible that it could be used to either protect a newer formulation of Pegasys or defensively to make life more difficult for biosimilar producers who would have to work around the patent for an alternative formulation.

At the time of writing, there is no PCT national phase data for this application. This is probably due to the PCT application having only been recently published and it can take some time before the national phase data becomes available. It is also possible that Roche may have elected to not pursue the application in any of the designated states/regions.

3.2 Schering-Plough/PegIntron

Product Background

The polymer used within PegIntron (PEG interferon alfa-2b) is a monomethoxy PEG in a ratio of 1:1 with the protein molecule. The conjugated product has an average molecular weight of 31,300 daltons, of which the molecular weight of the protein is 19,300 daltons.

Key Patents

The search identified 12 patents in the name of Schering that claim a form of PEG interferon alfa. The following patents are considered key for protecting the product PegIntron.

PEG interferon alpha conjugates for therapy of infection

This patent claims the method of treating patients using the molecular weight of PEG interferon alpha 2b as used in the marketed product, PegIntron. As such, this patent is key for the protection of PegIntron.

European/US/Pct Patent Nos.	Expected Expiry	Description/Claims based on EP/PCT Patents	Country Status
PCT/US98/07634 (WO98/48840) EP0858343 (Granted) EP0975369 (Granted) US5908621 (Granted) US6177074 (Granted) US6461605 (Granted) US6524570 (Granted)	28.4.2018	The main claim covers a method of treating a viral infection susceptible to treatment with interferon alfa comprising administering an amount of PEG 12000-inteferon alfa. This patent covers the method for treating patients using the molecular weight of PEG interferon alfa-2B as used in the marketed product PegIntron.	Brazil – Application abandoned Egypt – NA Georgia – No patent found Kyrgyz Republic –No patent found India – No equivalent/corresponding application found Indonesia – Application filed (current status not available) Russia – No patent found Thailand – NA Ukraine – No patent found

According to the search results, this patent was never filed in India and was abandoned by Schering in Brazil as a result of non-payment of renewal fees. No equivalent patents were found in Georgia, Kyrgyz Republic, Russia or Ukraine.

It is also believed that this application was not filed in Egypt, but further searches would need to be conducted to confirm this.[8]

[8] See Tahir Amin, Granted Pharmaceutical Patents in Egypt, I-MAK, December 2011 - available at http://tinyurl.com/7oukzst. This report reviews all granted pharmaceutical patents in Egypt between the periods 1 January 2005 to 31 December 2010.

With respect to Indonesia, an application appears to have entered the national phase, but there is no public data to confirm its current status.

Formulations for protection of pegylated-inteferon alpha conjugates

This patent covers aqueous formulations of PEG interferons. The excipients used in this formulation correspond to the summary of product characteristics (SmPC) listed for PegIntron. Biosimilar producers would have to use an alternative formulation to avoid infringing this patent.

European/US/Pct Patent Nos.	Expected Expiry	Description/Claims based on EP/PCT Patents	Country Status
PCT/US99/04268 (WO99/48535) EP1066059 (Granted) US6180096 (Granted) US6250469 (Granted) (The US patents have similar claims but are not part of patent family)	24.3.2019	The main claim covers an aqueous formulation comprising PEG interferon alfa conjugates, a buffer, a stabliser, a cryoprotecant and a solvent. This patent covers the current formulation used for the marketed product PegIntron.	Brazil – Application refused, appeal filed Egypt – NA Georgia – No patent found Kyrgyz Republic – No patent found India – Granted Indonesia – Application filed (current status not available) Russia – No patent found Thailand – Application filed (current status not available) Ukraine – No patent found

The equivalent patent was refused during examination in Brazil, but is now under appeal.

No equivalent patents were found in Georgia, Kyrgyz Republic, Russia or Ukraine.

In India, the patent has been granted as Patent No. 207233. A divisional patent deriving from granted patent 207233 has also ben granted under Patent No. 234103. Patent No. 207233 is the subject of the patent infringement case filed by Schering against Virchow Biotech and one of its distributors, Ranbaxy Inc.

Equivalent applications were also filed in Indonesia and Thailand, but there is no public data available to confirm their current status.

Stable pegylated interferon formulation

The patent describes stable formulations of PEG interferon conjugates with trehalose, which are stable at room temperature when lyophilized. Although the excipients claimed in this patent do not match those specified for the marketed

product PegIntron, it is possible that this patent could serve as a barrier to manufacturers when formulating a biosimilar version.

This application was granted in India as Patent No. 24176. Records show that Virchow Laboratories filed a pre-grant opposition against this application, which was ultimately unsuccessful due to late filing.

The application in Brazil is showing as abandoned but could be restored if Schering files the necessary request before 11 March 2013.

No equivalent patents were found in Georgia, Kyrgyz Republic, Russia or Ukraine.

European/US/Pct Patent Nos.	Expected Expiry	Description/Claims based on EP/PCT Patents	Country Status
PCT/US05/ 028441 (WO06/020720) EP1796647 (Granted) US7632491 (Granted)	11.8.2025	The main claim covers a solution for preparing a lyophilized powder formulation, the solution comprising PEG interferon, a cryoprotectant, a buffer, a stabiliser and water for injection, wherein trehalose comprises at least 60% by weight of the cryoprotectant, and the buffer maintains the PH of the formulation between 4.5. and 7.1. This patent appears to claim a more stable formulation for the marketed product PegIntron. The weight of the PEG inteferon-alfa 2B is 12000, as used in the PegIntron product, although the excipients claimed do not seem to match those specified in the product label.	Brazil – Abandoned (subject to restoration) Egypt – NA Georgia – No patent found Kyrgyz Republic – No patent found India – Granted Indonesia – NA Russia –No patent found Thailand – NA Ukraine – No patent found

Combination therapies comprising ribavirin and peginterferon alfa 2A or 2B

The search revealed various combination patents (see WO 99/59621, WO 99/15194, WO 00/37110 and WO 02/32414) claiming the use of ribavirin in combination with PEG interferon alfa 2A or 2B. While these patents are important when treating patients with HCV, the scope of the claims are limited to particular methods of treatment, such as administering ribavirin with an interferon alfa for a time period of 20 up to 50 weeks. As such, these patents should not be considered key in blocking the production of biosimilar PEG inteferon.

3.3 Enzon, Inc

The patent landscape includes three patents in the name of Enzon Inc, which are important for biosimilar production. Press statements show that in 1999 Enzon Inc entered into a licensing agreement with Schering for its branched PEG patents.[9] Following a patent dispute between Schering and Roche over their respective PEG interferon patents, an agreement was reached wherein Schering and Roche would cross-license to each other all patents applicable to their pegylated alpha interferon products. The agreement also included Schering sub-licensing Enzon's branched PEG patents to Roche.

The patent search identified three patents in the name of Enzon, Inc that are likely to be relevant to the licensing deal between Enzon, Schering and Roche and, therefore, the production of biosimilar versions of PegIntron and Pegasys.

Two of the patents (see WO95/13090 and WO 97/18832) cover processes for preparing long acting alfa interferon polymer conjugates and their compositions.

Patent number WO 99/32139 is particularly important as it covers improved interferon polymer conjugates, including the particular pegylated form used for PegIntron. Indeed, the equivalent US Patent No. 5951974 is listed on the PegIntron product label. Based on the conducted searches, this patent does not appear to have been filed in the countries covered by this landscape.

[9] Enzon Announces Schering-Plough In-licensing agreement with Roche Resolving Peginterferon Patent Disputes, 13 August 2001 available at http://investor.enzon.com/releasedetail.cfm?ReleaseID=138770

4. Methodology

Patent searches were conducted using the following databases for European, US and PCT patents:

Chemical Abstracts, Esp@cenet, WIPO Patentscope, Thomson Innovation (Derwent World Patent Index) and Health Canada.

Keywords used included: INTERFERON, PEGYLATED, PEG and HEPATITIS.

In addition, further restricted searches using the above keywords alongside Schering, Roche, Genentech, Merck and Enzon were conducted.

Once the relevant European, US and PCT patents were identified, the patent family for each relevant patent was reviewed to establish whether equivalent patents existed in the countries of interest. Where the patent family did not reveal such information, further searches were conducted using country patent office databases that are available. These included Brazil and India. Although Thailand also has a searchable database, it does not appear to be reliable or consistent in the results produced. As such this patent landscape does not incorporate results from the Thai Patent Office database. Patent information was sourced locally -- including patent documents where available -- for Georgia, Kyrgyz Republic, Russia and Ukraine.

As with all methodologies for patent searching, there are a number of limitations. First, despite efforts to conduct a comprehensive search, it is possible that some patents may have been missed. Given that patent applications are usually published 18 months from the earliest filing date, patents that fall within this window were not captured. Public patent databases may not always be current and information obtained from the databases used may have errors. However, all precautions have been taken to ensure that the information made available in this patent landscape is as accurate as possible based on the sources available.

Annex I: Patent Landscape

Hoffman-La Roche (including Genentech)/Pegasys

US/EPO/ PCT Patent Nos.	Expected Expiry	Title/Description/Claims/Comment Based on European/PCT patents	Brazil	Egypt	Georgia	Kyrgyz Republic	India	Indonesia	Russia	Thailand	Ukraine
EP0510356 (Granted) US5539063 (Granted) 5559213 (Granted) 5595732 (Granted) 5747646 (Granted) 5792834 (Granted) 5834594 (Granted) 5849860 (Granted) No PCT application filed	18.3.2012	***Polyethylene glycol protein conjugates*** The patent describes an invention for providing a physiologically active conjugate of interleukin and interferon-alpha (IFN-α) proteins. The key claims cover a physiologically active conjugate of interleukin and IFN- α proteins, wherein the polyethylene glycolation pegylation residue(s) per protein is from 300-30,000 daltons. Claim 12 of the European patent specifies the protein conjugate as IFN- α. Although this patent claims the pegylation of IFN- α, the molecular weight and process set out in the here reportedly resulted in a low yield and lowered the potency of the pegylated molecule. **This patent does not cover the current marketed product Pegasys.**	PI9201015 **(Application refused - appeal filed, refusal maintained)**	NA	NA	NA	No patent found	NA	NA	NA	NA

US/EPO/ PCT Patent Nos.	Expected Expiry	Title/Description/Claims/Comment Based on European/PCT patents	Brazil	Egypt	Georgia	Kyrgyz Republic	India	Indonesia	Russia	Thailand	Ukraine
EP0593868 (Granted) US5382657 (Granted) No PCT application filed	13.8.2013	***Peg-interferon conjugates*** This patent describes an invention for IFN-polyethylene glycol (PEG) conjugates, with unique linkers, which connect an IFN amino group to PEG. The main claim covers an interferon conjugate where the molecular weight of the polymeric unit in the conjugate is in the range of about 1000 daltons to 10,000 daltons. Claim 4 and 5 claim the molecular weight of the polymeric unit in the conjugate in the range of 1000-5000 daltons or 1000-2200 daltons. Claim 8 covers an interferon conjugate of the main claim, wherein the IFN is interferon α2A. Claim 16 covers a process for the preparation of an interferon conjugate, including IFN α2A. Claims 17-19 cover pharmaceutical compositions comprising interferon conjugates claimed herein. **This size of the PEG claimed here is not as used in the marketed product Pegasys. This patent does not, therefore, specifically cover the marketed product Pegasys and is not a key patent for infringement purposes. However, the patent may be used a defensively such as to broaden the**	PI9303469 **(Application refused - appeal filed, refusal maintained)**	NA	NA	NA	No patent found	NA	NA	NA	NA

US/EPO/ PCT Patent Nos.	Expected Expiry	Title/Description/Claims/Comment Based on European/PCT patents	Brazil	Egypt	Georgia	Kyrgyz Republic	India	Indonesia	Russia	Thailand	Ukraine
		scope of protection around the key patent covering Pegasys (see EP0809996 below).									
EP0809996 (Granted) US7201897 (Granted) No PCT application filed	22.5.2017	***Interferon Conjugates*** This patent describes an invention for a specific branched PEG conjugate structure, which is claimed to increased circulating half-life and plasma residence time, reduced immunogenicity, decreased clearance and increased antiproliferative activity compared to unmodified IFN α and greater antiproliferative activity and virtually no immunogenicity compared to other PEG-IFN α conjugates. The main claim covers a physiologically active pegylated IFNα conjugate wherein the average molecular weight of the PEG units in the said conjugate is from 26,000-66,000 daltons. Claims 2 and 3 cover a molecular weight of the PEG units from 35-45,000 and 40,000 daltons. Claim 6 claims the conjugate of the main claim wherein the IFNα is IFN α2a. Claim 11 covers a method for producing a PEG IFN α conjugate consisting of covalently linking a reagent to formula II. Claims 12-13 cover pharmaceutical compositions comprising a PEG IFN α claimed herein. **This patent covers the marketed product Pegasys. The patent is the key patent for**	PI9703421 **(Granted)**	EG24292 (**Granted)**	GE1648 (**Granted)**	KG338 (**Granted)**	198952 **(Granted patent revoked on appeal)** 1831/CHE/ 2005 **(Divisional application of 198952 – application withdrawn)**	NA	RU2180595 (**Granted)** Claims reflect those as granted in Europe	NA	UA56989 **(Granted)**

US/EPO/ PCT Patent Nos.	Expected Expiry	Title/Description/Claims/Comment Based on European/PCT patents	Brazil	Egypt	Georgia	Kyrgyz Republic	India	Indonesia	Russia	Thailand	Ukraine
		infringement purposes. The molecular weight ranges for PEG claimed in this patent relate to the size of the PEG used in the Pegasys product i.e. approximately 20-60,000 daltons (as referred to in product's packaging label).									
PCT/EP99/03746 (WO99/64016) EP1087778 (Granted) US20030053986 US20050031589 US20070196385 (Abandoned)	29.5.2019	***Use of PEG-IFN-Alpha and Ribavirin for the treatment of chronic hepatitis C*** This patent describes the use of PEG-IFN α conjugates in association with ribavirin for the manufacture of medicaments to treat chronic hepatitis C infections. The main claim covers the use of PEG-IFN α in association with ribavirin for the manufacture of a medicament for the treatment of chronic hepatitis C. Claim 2 covers the use according to the main claim where the amount of PEG-IFN α conjugate is about 33 to 540mcg per week. Claim 3 covers the use according to the main claim where the amount of ribavirin is 400 to 1200mg daily. Claim 4 claims the use according to the claims above wherein the PEG-IFN α conjugate is PEG-IFN α2A as patented in EP 0809996 (Roche's key patent for PEG-IFN α). The remaining claims relate to methods of use.	PI9911076 **(Application refused - appeal filed)**	NA	No patent found	No patent found	233722 **(Granted)** The 3 granted claims in India cover a composition for the treatment of chronic hepatitis C comprising PEG-IFN α2A with ribavirin. The amount of PEG-IFN α2A conjugates in the composition is 33 to 540 mcg per week with 400 to 1200 mg of ribavirin daily.	29285 **(Pending current status not available)**	2271217 **(Granted)** Claims mirror those as granted in Europe	050925 **(Pending current status not available)**	No patent found

US/EPO/ PCT Patent Nos.	Expected Expiry	Title/Description/Claims/Comment Based on European/PCT patents	Brazil	Egypt	Georgia	Kyrgyz Republic	India	Indonesia	Russia	Thailand	Ukraine
		This patent provides protection for the use of Pegasys (PEG-IFN α/ PEG-IFN α2A) with ribavirin to treat chronic hepatitis C.									
PCT/EP00/07666 (WO01/12214) EP1220683 (Withdrawn) US20010046957 Abandoned)	8.8.2020	***Mycophenolate mofetil in association with PEG-IFN α*** This patent describes the use of IFN- α (including PEG IFN α or PEG IFN α2A) in association with a pharmaceutically acceptable salt or a prodrug of mycophenolic acid for the manufacture of medicaments for treating liver disease patients, in particular chronic viral hepatitis C. The main claim covers the use of a therapeutically effective amount of IFN α or PEG-IFN α in association with a therapeutically effective amount of a pharmaceutically acceptable salt or prodrug of mycophenolic acid for the manufacture of medicaments for treating liver diseases. Claim 12 covers medicaments combining a pharmaceutically acceptable salt or prodrug of mycophenolic acid with PEG-IFN α2A. **This patent covers the use of IFN- α (including PEG IFN α or PEG IFN α2A) with a pharmaceutically acceptable salt or a prodrug of mycophenolic acid. Mycophenolate mofetil is marketed by Roche as Cellcept for use as an immunosuppressant.**	PI0013252 **(Application abandoned)**	NA	NA	NA	No patent found	NA	2002105485 **(Application withdrawn)**	NA	NA

US/EPO/ PCT Patent Nos.	Expected Expiry	Title/Description/Claims/Comment Based on European/PCT patents	Brazil	Egypt	Georgia	Kyrgyz Republic	India	Indonesia	Russia	Thailand	Ukraine
EP0736303 (Granted) US5762923 (Granted) No PCT application filed	30.3.2016	**Interferon solution** This patent describes an aqueous solution of interferon alpha (preferably PEG IFN α2A), which is suitable for parenteral administration. The claims cover an aqueous IFN solution containing an IFN-α, IFN-α-2a or PEG-IFN α2A with a non-ionic detergent, a buffer for adjusting pH 4.4-5.5, benzyl alcohol and an isotonizing agent. **This patent appears to cover the excipients/formulation as used in the marketed product Pegasys.**	PI9601276 **(Application suspended pending response to examination report by the applicant)** The claims as filed in the Brazilian application mirror the European patent claims	NA	No patent found	No patent found	234072 **(Granted)** Claims identical to those as granted for EP0736303	NA	2113845 **(Granted)**	NA	No patent found
PCT/EP2003/012498 (WO04/045648) EP1562634 (Granted) US20040223950 (Abandoned)	10.11.2023	***Positional isomers of PEG IFN Alpha 2A*** This patent describes positional isomers of monopegylated IFN-α2A, including the method for isolation and their use in the manufacture of medicaments for the treatment of illnesses, especially for the treatment of viral diseases. The key claims cover positional isomers of PEG IFN-α2A with 9 possible lysine residues as conjugation sites and the method for their isolation. **This patent does not relate to the marketed product Pegasys.**	PI0316227 **(Application abandoned)**	NA	NA	NA	No patent found	NA	2005118752 **(Application withdrawn)**	NA	NA
PCT/EP2008/004165 (WO08/145323)	25.5.2028	***Pharmaceutical formulation for interferons*** The patent describes a pharmaceutical formulation comprising IFN-α (including PEG	National phase data currently not available or applicant has	National phase data currently not available or	National phase data currently not available or	National phase data currently not	National phase data currently not available or	National phase data currently not	National phase data currently not available or applicant has	Information not available (Thailand not designated	National phase data currently not available or

US/EPO/ PCT Patent Nos.	Expected Expiry	Title/Description/Claims/Comment Based on European/PCT patents	Brazil	Egypt	Georgia	Kyrgyz Republic	India	Indonesia	Russia	Thailand	Ukraine
		IFN- α) as an active agent and anti-oxidant. The key claims cover a pharmaceutical formulation comprising an IFN-α (including a PEG IFN-α conjugate) as active agent and an anti-oxidant for treating hepatitis C. **This patent claims to be an improved formulation over the one currently used for Pegasys (see EP0736303 above), but is not used for marketing.**	elected to not pursue the application into the national phase	applicant has elected to not pursue the application into the national phase	applicant has elected to not pursue the application into the national phase	available or applicant has elected to not pursue the application into the national phase	applicant has elected to not pursue the application into the national phase	available or applicant has elected to not pursue the application into the national phase	elected to not pursue the application into the national phase	in PCT application)	applicant has elected to not pursue the application into the national phase
PCT/EP2009/ 066567 (WO10/069809) EP2379745 (Pending) US20100158866 (Pending)	8.12.2029	***Biomarkers for HCV treatment response*** This patent relates to methods that are useful for predicting the response of hepatitis C virus infected patients to pharmacological treatment. The key claims cover a method for predicting the response of a human subject infected with the hepatitis C virus to a treatment with interferon, including the product Pegasys. **This patent, while referencing PEG IFN-α2A in the claims, is limited to the method claimed in the patent for predicting the response of patients on Pegasys.**	National phase data currently not available	National phase data currently not available	National phase data currently not available	National phase data currently not available	1171/MUMNP/2011 **(Pending)** The claims filed in India are as filed for the PCT application	National phase data currently not available	National phase data currently not available	National phase data currently not available	National phase data currently not available

US/EPO/ PCT Patent Nos.	Expected Expiry	Title/Description/Claims/Comment Based on European/PCT patents	Brazil	Egypt	Georgia	Kyrgyz Republic	India	Indonesia	Russia	Thailand	Ukraine
PCT/US09/ 068556 (WO10/080528) EP2376117 (Pending) US20120027722 (Pending) *This patent is filed in the name of Genentech, Inc and the Medical Research Council	17.12.2029	***Hepatitis C virus combination therapy*** This patent describes methods and compositions for the treatment or prevention of hepatitis C comprising the administration of a combination of anti-hepatitis C virus antibodies and α-IFN. The claims cover a method of treating or preventing a hepatitis C virus infection in a subject comprising administering to the individual an effective amount of a composition comprising an anti-HCV antibody that binds hepatitis E2 protein and an effective amount of α-IFN, including PEG IFN-α2. **This patent, while referencing PEG IFN-α2A in the claims, is limited to the method claimed in the patent for treating hepatitis C with an effective amount of an anti-HCV antibody that binds E2 protein and effective amount of α-IFN. As this patent does not cover the marketed product Pegasys.**	National phase data currently not available	National phase data currently not available	National phase data currently not available	National phase data currently not available	4984/CHENP/ 2011 **(Withdrawn)**	National phase data currently not available	National phase data currently not available	National phase data currently not available	National phase data currently not available

Schering Corporation (including Merck & Co, Inc)/PegIntron

US/EPO/ PCT Patent Nos.	Expected Expiry	Title/Description/Claims/Comment Based on European/PCT patents	Brazil	Egypt	Georgia	Kyrgyz Republic	India	Indonesia	Russia	Thailand	Ukraine
PCT/US98/07634 (WO98/48840) EP0858343 (Granted) EP0975369 (Granted) US5908621 (Granted) US6177074 (Granted) US6461605 (Granted) US6524570 (Granted)	28.4.2018	***Polyethylene glycol-interferon alpha conjugates for therapy of infection*** This patent describes a method of treating viral infections, in particular viral infections that are susceptible to treatment with IFN-α, comprising the administration of a PEG IFN- α conjugate. The main claim covers a method of treating a viral infection susceptible to treatment with IFN- α comprising administering an amount of PEG 12000-IFN α. Claims 2 and 3 claim the method of the main claim but where the PEG 12000-IFN α is either PEG 12000-IFN α-2A or PEG 12000-IFN α-2B. **This patent covers the method for treating patients using the molecular weight of PEG-IFN α-2B as used in the marketed product PegIntron.**	PI9809425 **(Application abandoned)**	NA	No patent found	No patent found	No patent found	22977 **(Pending – current status not available)**	No patent found	NA	No patent found
PCT/US99/04268 (WO99/48535) EP1066059 (Granted) US6180096 (Granted)	24.3.2019	***Formulations for protection of PEG-IFN Alpha conjugates*** This patent describes formulations that permit the stablisation of PEG-IFN α conjugates during and after lyphilisation. The main claim covers an aqueous	PI9909087 **(Application refused-appeal filed)**	NA	No patent found	No patent found	207233 **(Granted)** This patent is the subject of the patent infringement case filed	28470 **(Pending – current status not available)**	No patent found	049580 **(Pending – current status not available)**	No patent found

US/EPO/ PCT Patent Nos.	Expected Expiry	Title/Description/Claims/Comment Based on European/PCT patents	Brazil	Egypt	Georgia	Kyrgyz Republic	India	Indonesia	Russia	Thailand	Ukraine
US6250469 (Granted) (The US patents have similar claims but are not part of patent family)		formulation comprising PEG-IFN α conjugates, a buffer, a stabliser, a cryoprotecant and a solvent. Claim 6 claims the formulation herein but where the PEG IFN-α molecules are selected from the group consisting of IFN- α 2A, 2B and 2C and consensus IFN. Claim 7 specifies the PEG at 12000. **This patent covers the current formulation used for the marketed product PegIntron.**					against Virchow Labs and Ranbaxy 234103 **(Granted)** This patent is a divisional of Patent No. 207233.				
PCT/US99/07037 (WO99/59621) PCT/US98/18488 (WO99/15194) EP1136075 (Granted) EP1213029 (Pending) EP1317929 (Withdrawn) EP2305287 (Pending) EP903148 (Granted) EP956861 (Granted)	13.5.2019	*Two PCT patents were identified in the same family. Only by reviewing the actual claims in a designated country will it be possible to determine which application relates to the local patent number entered at the national phase. Below is a summary of each PCT application. ***WO99/59621*** ***Combination therapy comprising ribavirin and interferon alpha in antiviral treatment naive patients having chronic hepatitis C infection*** This patent describes the uses of ribavirin and IFN- α to prepare pharmaceutical compositions. The main claim covers the use of ribavirin for the manufacture of a pharmaceutical composition comprising the administering of ribavirin with IFN- α for time period of 20 up to 50 weeks.	PI9812484 **(Application refused – no status as to whether period to appeal has expired)** PI9910505 **(Application refused – period for appeal expired)**	NA	NA	NA	No patent found	NA	NA	NA	NA

US/EPO/ PCT Patent Nos.	Expected Expiry	Title/Description/Claims/Comment Based on European/PCT patents	Brazil	Egypt	Georgia	Kyrgyz Republic	India	Indonesia	Russia	Thailand	Ukraine
US6172046 (Granted) US6472373 (Granted) US20030039630 (Abandoned) US20060257365 (Abandoned)		Claim 9 specifies the use of IFN- α is selected from IFN- α 2A, 2B, a consensus IFN, purified IFN product, PEG-IFN- α 2A/2B. ***WO99/15194*** ***Combination therapy for eradicating detectable HCV-RNA in patients having chronic hepatitis C infection*** This patent describes the use of ribavirin with IFN-α for the manufacture of pharmaceutical compositions for patients that have failed to respond to a previous course of IFN- α. The main claim covers the use of ribavirin for the manufacture of a pharmaceutical composition to be administered with an effective amount of IFN- α Claim 8 covers the use of a PEG-IFN- α, including PEG IFN- IFN- α 2B. **These patents cover methods of use for administering ribavirin and PEG-IFN- α 2B. These patents are not key in blocking the use of a biosimilar version of PegIntron with ribavirin, provided the method of treatment is not as claimed herein.**									
PCT/US99/27934 (WO00/37097)	16.12.2019	***Ribavirin-interferon alfa induction HCV combination therapy*** This patent describes the use of ribavirin for the manufacture of a pharmaceutical composition with an effective amount of	No patent found	NA	NA	NA	No patent found	NA	NA	NA	NA

US/EPO/ PCT Patent Nos.	Expected Expiry	Title/Description/Claims/Comment Based on European/PCT patents	Brazil	Egypt	Georgia	Kyrgyz Republic	India	Indonesia	Russia	Thailand	Ukraine
		IFN-α for a period of at least 20-30 weeks. The main claim covers the use of ribavirin for the manufacture of a pharmaceutical composition with an effective amount of IFN-α for a period of at least 20-30 weeks. **The scope of this patent is limited to the particular method of use claimed. The claims do not claim the method of use with a PEG-IFN- α. If granted, this is not a key patent for preventing biosimilar production.**									
PCT/US99/27935 (WO00/37110) EP1140143 (Withdrawn)	16.12.2019	***Ribavirin-interferon alfa induction HCV combination therapy*** This patent describes the use of ribavirin, PEG IFN- α and combinations for the manufacture of pharmaceutical compositions for treating patients with chronic hepatitis C. The main claim covers the use of ribavirin for the manufacture of a pharmaceutical composition for treating a patient having a chronic hepatitis C infection to eradicate HCV-RNA by a method comprising administering ribavirin with PEG-IFN- α including within specified time periods of at least 20-30 weeks to reduce viral road and then HCV-RNA. Claim 8 specifies the particular use of PEG-IFN- α 2A or 2B, while claim 9 covers only the use of PEG-IFN-α 2B. **The scope of this patent is limited to the**	No patent found	NA	NA	NA	No patent found	NA	NA	NA	NA

US/EPO/ PCT Patent Nos.	Expected Expiry	Title/Description/Claims/Comment Based on European/PCT patents	Brazil	Egypt	Georgia	Kyrgyz Republic	India	Indonesia	Russia	Thailand	Ukraine
		particular method of use for ribavirin in combination with PEG-IFN-α. If granted, this is not a key patent for preventing biosimilar production.									
PCT/US00/10240 (WO00/62799) EP1046399 (Withdrawn)	18.4.2020	***HCV Combination therapy, containing ribavirin in association with antioxidants*** This patent describes the use of an antioxidant for the preparation of a medicament for ameliorating ribavirin-related hemolysis associated with the treatment of a chronic HCV infection with a combination therapy of IFN- α and ribavirin. Claim 3 covers the use of an antioxidant for the preparation of a medicament for ameliorating ribavirin-related hemolysis associated with the treatment of a chronic HCV infection with a combination therapy of PEG IFN- α 2A or 2B and ribavirin. **The scope of this patent is limited to the use of an antioxidant for preparing a medicament amerliorating ribavirin related hemolysis in combination with an IFN- α, including PEG IFN- α. If granted, this is not a key patent for preventing biosimilar production.**	PI0009840 **(Application abandoned)**	NA	NA	NA	No patent found	NA	NA	NA	NA
PCT/US01/32434 (WO02/32414) EP1326594 (Withdrawn) US20020127203 (Abandoned)	16.10.2021	***Ribavirin pegylated interferon alfa HCV combination therapy*** This patent describes the use of ribavirin and PEG IFN- α for the preparation of a pharmaceutical composition comprising an effective amount of ribavirin and PEG IFN- α for e treatment time period sufficient to eradicate detectable HCV-RNA and to	PI0114636 **(Application abandoned)**	NA	NA	NA	No patent found	NA	NA	NA	NA

US/EPO/ PCT Patent Nos.	Expected Expiry	Title/Description/Claims/Comment Based on European/PCT patents	Brazil	Egypt	Georgia	Kyrgyz Republic	India	Indonesia	Russia	Thailand	Ukraine
		maintain no detectable HCV-RNA for a period of at least 12 weeks after the end of the treatment time period. The main claim broadly covers the use of ribavirin for the preparation of a pharmaceutical composition comprising also a therapeutically effective amount of PEG IFN- α. Claim 6 specifies the use of PEG IFN- α 2A or 2B. The subsequent claims then specify the particular weight of the dose for ribavirin and PEG IFN-α. **This patent covers ribavirin and PEG IFN- α (including 2A or 2B) as a single dosage form. This patent should not be key to blocking a biosimilar product if granted.**									
PCT/US01/12760 (WO01/81359) EP1282632 (Withdrawn) US6924270 (Granted) US7115578 (Granted)	18.4.2021	***Ribavirin-interferon alfa combination therapy for eradicating detectable HCV-RNA in patients having chronic hepatitis c infection*** This patent describes ribavirin derivative compounds and their use in pharmaceutical compositions with IFN- α, including PEG IFN-α 2A or 2B. Claims 1 and 2 cover a derivative compound of ribavirin and a pharmaceutical composition of the derivative. Claim 4 covers the use of the ribavirin derivative compound in association with	No patent found	NA	NA	NA	No patent found	NA	NA	NA	NA

US/EPO/ PCT Patent Nos.	Expected Expiry	Title/Description/Claims/Comment Based on European/PCT patents	Brazil	Egypt	Georgia	Kyrgyz Republic	India	Indonesia	Russia	Thailand	Ukraine
		IFN- α. Claim 9 specifies the possible use of PEG IFN- α 2a or 2B. **The scope of this patent is limited to the combination of the ribavirin derivative compound in combination with a IFN- α (including either PEG IFN- α 2a or 2B). This patent should not pose a barrier to biosimilar production if granted.**									
PCT/US05/ 028441 (WO06/020720) EP1796647 (Granted) US7632491 (Granted)	11.8.2025	***Stable pegylated interferon formulation*** This patent describes stable formulations of PEG-IFN conjugates with trehalose, which are stable at room temperature when lyophilized. The main claim covers a solution for preparing a lyophilized powder formulation, the solution comprising PEG IFN, a cryoprotectant, a buffer, a stabiliser and water for injection, wherein trehalose comprises at least 60% by weight of the cryoprotectant, and the buffer maintains the PH of the formulation between 4.5. and 7.1. Claim 14 specifies the use of PEG 12000-IFN- α 2B. **This patent appears to claim a more stable formulation for the marketed product PegIntron. The weight of the PEG IFN- α 2B is 12000, as used in the PegIntron product, although the excipients claimed do not seem to match those specified in the**	PI0513332 **(Abandoned – subject to restoration)**	NA	No patent found	No patent found	241476 **(Granted)** (Virchow Labs filed a pre-grant opposition against this application but it appears the applicant was notified of the opposition by the patent office after the patent had already been granted. A hearing was held but the Controller's decision is not publicly available).	NA	No patent found	NA	No patent found

US/EPO/ PCT Patent Nos.	Expected Expiry	Title/Description/Claims/Comment Based on European/PCT patents	Brazil	Egypt	Georgia	Kyrgyz Republic	India	Indonesia	Russia	Thailand	Ukraine
		product label. It is possible that this patent could be an issue for biosimilar manufacturers like Virchow if there are no alternatives to formulating a similar stable product as claimed in this patent.									
PCT/US99/20900 (WO00/29440) EP1894944 (Granted) US6281337 (Granted)	5.10.2019	***Methods of conversion of interferon isoforms and products thereof*** This patent describes methods for preparing highly purified proteins for increasing the yield of an IFN- α composition, comprising converting an adjunct isoform into IFN- α, with a preferred use of IFN- α 2B. The main claim covers a method for increasing the yield of an IFN- α composition comprising an adjunct isoform into IFN- α. Claim 3 specifies the IFN- α as IFN- α 2B. **The scope of this patent is limited to the method of increasing the yield of and IFN- α composition where an adjunct isoform is converted into IFN- α. This patent does not make any claims in relation to PEG IFN- α 2B and is not a related to the PegIntron product.**	PI9915257 **(Application suspended pending response to examination report by applicant)**	NA	NA	NA	199135 **(Granted)**	28552 **Pending – current status not available)**	NA	NA	NA
PCT/US99/21448 (WO00/23454) PCT/US99/21450 (WO00/23455) EP1121369 (Granted) EP1121370 (Withdrawn)	14.10.2019	*Two PCT patents were identified in the same family. Only by reviewing the actual claims in a designated country will it be possible to determine which application relates to the local patent number entered at the national phase. Below is a summary of each PCT application. ***WO00/23454*** ***Ribavirin-interferon alfa combination***	PI9915546 **(Application abandoned)**	Information not available	Information not available	Information not available	No patent found	29187 **(Current status not available)**	2001113268 **(Application withdrawn)**	NA	NA

US/EPO/ PCT Patent Nos.	Expected Expiry	Title/Description/Claims/Comment Based on European/PCT patents	Brazil	Egypt	Georgia	Kyrgyz Republic	India	Indonesia	Russia	Thailand	Ukraine
US6277830 (Granted)		***therapy for eradicating detectable HCV-RNA in patients having chronic hepatitis C infection*** This patent describes methods for treating chronic hepatitis C by administering a therapeutically effective amount of ribavirin and IFN-α for a particular time period sufficient to eradicate HCV-RNA, including also ribavirin derivatives. The main claim covers the use of a ribavirin derivative compound for the preparation of a pharmaceutical composition by administering it with a therapeutically effective amount if IFN- α for period of time sufficient to eradicate detectable HCV-RNA and to have no detectable HCV-RNA for at least 24 weeks after the said period of administering the composition. Claim 7 specifies the use of IFN- α 2A 2B or a PEG IFN. ***WO0023455*** ***Ribavirin-interferon alfa combination therapy for eradicating detectable HCV-RNA in patients having chronic hepatitis C infection*** This patent describes a ribavirin derivative compound wherein at least one functional group is a straight or branched polyalkylene oxide polymer conjugate, and pharmaceutical compositions alone and in combination with IFN-α.									

US/EPO/ PCT Patent Nos.	Expected Expiry	Title/Description/Claims/Comment Based on European/PCT patents	Brazil	Egypt	Georgia	Kyrgyz Republic	India	Indonesia	Russia	Thailand	Ukraine
		The main claims covers a ribavirin derivative compound wherein at least one functional group is a straight or branched polyalkylene oxide polymer conjugate. Claim 18 covers the use of the ribavirin derivative with IFN- α, including either PEG IFN- α 2A or 2B or a PEG IFN- α. **Neither of these patents covers the currently marketed product PegIntron.**									

Enzon Inc

US/EPO/ PCT Patent Nos.	Expected Expiry	Title/Description/Claims/Comment Based on European/PCT patents	Brazil	Egypt	Georgia	Kyrgyz Republic	India	Indonesia	Russia	Thailand	Ukraine
PCT/US94/13207 (WO95/13090) EP0730470 (Granted) US5711944 (Granted)	10.11.2014	***Improved interferon polymer conjugates*** This patent describes a process for preparing long acting α-IFN containing compositions. The main claim covers a process for preparing a long-acting α-IFN containing composition, comprising contacting α-IFN with a substantially non-antigenic polymer in the presence of a surfactant under conditions which are sufficient to effect conjugation of the protein and polymer. Claims 32 and 33 cover a product based on the process claimed in the main claim. **This patent may be relevant to the production of PegIntron in so far as Schering and Enzon entered into a licensing agreement for use of Enzon's α-IFN conjugation patents. Enzon's PEG-IFN patents formed part of the subsequent litigation between Schering and Roche which was subsequently settled in 2001 through Schering providing a sub-license of Enzon's PEG patents to Roche as well as Schering and Roche agreeing to cross license to each other all patents applicable to their PEG IFN-α patents for PegIntron and Pegasys.**	No patent found	NA	NA	NA	No patent found	NA	NA	NA	NA

US/EPO/ PCT Patent Nos.	Expected Expiry	Title/Description/Claims/Comment Based on European/PCT patents	Brazil	Egypt	Georgia	Kyrgyz Republic	India	Indonesia	Russia	Thailand	Ukraine
PCT/US96/17448 (WO97/18832) EP0862455 (Granted) US5738846 (Granted)	31.10.2016	***Interferon-polymer conjugates and process for preparing the same*** This patent describes a process for preparing long acting IFN containing compositions. The main claim covers a process for preparing IF-polymer conjugates by reacting an IFN with a bis-activated substantially non-antigenic polymer in a molar ratio of substantially non-antigenic polymer to IFN of from about 0.125:1 to about 1:1 under conditions sufficient to effect covalent conjugation of said IFN and said polymer and form a reaction mixture containing mono-IFN polymer conjugates and bis-IFN conjugates. Further claims cover compositions of IFN, mono-IFN, bis-IFN conjugates and polymers according to specific ratios and weight. **This patent may be relevant to the production of PegIntron in so far as Schering and Enzon entered into a licensing agreement for use of Enzon's α-IFN conjugation patents. Enzon's PEG-IFN patents formed part of the subsequent litigation between Schering and Roche which was subsequently settled in 2001 through Schering providing a sub-license of Enzon's PEG patents to Roche as well as Schering and Roche agreeing to cross license to each other all patents applicable to their PEG IFN-α patents for PegIntron and Pegasys.**	No patent found	NA	NA	NA	No patent found	NA	NA	NA	NA

US/EPO/ PCT Patent Nos.	Expected Expiry	Title/Description/Claims/Comment Based on European/PCT patents	Brazil	Egypt	Georgia	Kyrgyz Republic	India	Indonesia	Russia	Thailand	Ukraine
PCT/US98/26677 (WO99/32139) EP1039922 (Granted) US5951974 (Granted) US6042822 (Granted)	16.12.2018	***Improved interferon polymer conjugates*** This patent includes pharmaceutical compositions containing a mixture of mono-polymer stranded α-IFN conjugates. The main claim covers a pharmaceutical composition comprising a mixture of α-IFN polymer conjugate positional isomers, wherein one of the said positional isomers comprises an α-IFN covalently conjugated to a substantially non-antigenic polymer at a histidine residue on said α-IFN. Claim 2 covers the main claim wherein the said α-IFN is IFN- α 2B. Claim 9 and 10 cover the said pharmaceutical compositions wherein the polyalkylene oxide is PEG or a monomethoxy-polyethylene glycol (mPEG). **This patent is listed on the PegIntron packaging label. This patent is likely to have formed part of the licensing agreement between Schering and Enzon and is therefore, relevant for any biosimilar production.**	No patent found	NA	No patent found	No patent found	No patent found	NA	No patent found	No patent found	No patent found