Amgen, Inc. Response to the European Commission Public Consultation

May 9, 2008

PUBLIC CONSULTATION IN PREPARATION OF A LEGAL PROPOSAL TO COMBAT COUNTERFEIT MEDICINES FOR HUMAN USE

KEY IDEAS FOR BETTER PROTECTION OF PATIENTS AGAINST THE RISK OF COUNTERFEIT MEDICINES

Introduction and Summary

Amgen is a leading human therapeutics company in the biotechnology industry. For more than 25 years we have focused on accomplishing our mission to serve patients by discovering, developing and delivering innovative medicines to treat grievous illnesses. By pioneering the development of novel products based on advances in recombinant DNA and molecular biology, Amgen's therapeutics have changed the practice of medicine and helped millions of people around the world to fight cancer, kidney disease, rheumatoid arthritis and other serious illnesses.

Amgen provides millions of units of medicine annually to improve the lives of patients in the 27 EU countries.

Amgen takes the issue of counterfeit drugs very seriously and is committed to the highest standards of drug quality and patient safety. Our brand protection program supports an effective, secure and resilient global supply chain and the overall integrity of Amgen's medicines for the protection and safety of patients.

Since the year 2000, Amgen has experienced three separate counterfeiting attacks on its products and patients. The experience we gained in defending against these criminal attacks has given us a particular perspective on and sensitivity to the issues that the Commission is seeking comment on in this Consultation.

In general, Amgen feels biotech medicines (recombinant proteins) need special attention when it comes to designing anti-counterfeiting measures, for a number of reasons:

- Biotech medicines typically treat serious, often life threatening diseases – for a patient obtaining a false copy this may have fatal consequences.
- Often biotech medicines are expensive, and therefore may be a particularly attractive target for counterfeiters.
- Many biotech medicines can degrade if not maintained in a cold chain environment, making them more sensitive to potential degradation if not properly handled.
- Biotech medicines are generally clear liquid injectables, whose authenticity is assured primarily by their delivery devices and packaging materials, making the protection of these features all the more essential for patient safety.

Amgen applauds the efforts of the Commission to increase the protection of patients from the acts of criminals and others who would attempt to insert counterfeit or substandard products into the medicine supply.

Specifically, Amgen believes that sealing the outer packaging of a medicine and ensuring that there is no intrusion into, over-packaging or repackaging of its contents is an essential element in preventing a range of counterfeiting attacks. While Amgen believes that this approach should be legally protected for all medicines, we think it is imperative in the case of injectable biological medicines. Additionally, we support the ultimate adoption of a "sealed and serialized" approach based on the use of legally protected sealing of outer packaging to ensure the physical integrity of the packaged medicine, and serialization of the package to ensure the source and authenticity of the packaged product.

Of course, there are a number of other important measures that are needed to further ensure the safety of medicines from counterfeiters. Amgen believes that the Commission has already identified a number of these and we support their adoption, together with certain additional steps that were not raised in the Consultation document.

Amgen's Experience Supports the Use of Legally Protected Tamper-evident Security Seals on the Outer Packaging of Medicines (Section 4.1.3)

During the period 2000-2002, Amgen experienced two separate counterfeiting attacks in the US on its product EPOGEN® (Epoetin alfa).[1] These incidents illustrate how the use of outer packaging, tamper-evident, security seals help protect against tampering related counterfeiting.

In August 2000, Amgen determined that a number of vials of its EPOGEN product had been tampered, the original contents withdrawn and replaced with an unknown substance and resold. At that time, EPOGEN outer packaging did not employ a tamper-evident security seal and the counterfeiters made use of the original packaging to sell the tampered product.

In May 2002, a second tampering-based counterfeiting attack took place. Criminals acquired EPOGEN product packaged in sealed tamper-evident outer boxes. They removed the vials from the original outer packaging, removed the vial labels and/or relabeled the product to mimic a more expensive, higher dose SKU. Due in part to the secure, tamper-evident Carton Closure Label (CCL) that Amgen had begun using on its secondary packaging, the product could not be packaged in the original outer box (i.e. Dispensing Pack). In their attempt to duplicate the genuine Amgen Dispensing Pack, they failed to duplicate the secure, color-shifting CCL. This gave a basis for Amgen, medical professionals, law enforcement and others to distinguish genuine from fake.[2]

[1] In addition to the two incidents of EPOGEN® counterfeiting, a second product, NEUPOGEN® (Filgrastim) was also attacked. In this case, however, the criminals used original components to fabricate the counterfeit product.

[2] MedWatch: 2002 Safety Alert-Epogen (Epoetin alfa), May 8, 2002 (http://www.fda.gov/medwatch/SAFETY/2002/epogen.htm)

Based on these counterfeiting incidents, Amgen is convinced that the secure outer box tamper-evident seal helped to limit the extent of counterfeiting in two ways: 1) the seal helped make reuse of the Dispensing Pack outer box impractical, and 2) the seal provided a basis for distinguishing the genuine from fake, thereby helping to protect patients.

Amgen uses this tamper-evident CCL security seal on all of its US injectable products to protect the integrity of its medicines for patients. We have begun adopting this security feature for certain international markets but are concerned that under current EC law this protection can be subverted through repackaging. By adopting legislation that prohibits the intrusion or obscuring of this feature, sealed Amgen products would better protect patients in two ways. First, medicines would be protected against counterfeiting by helping to ensure that the security features remain visible and that tampered or counterfeit product is not substituted for genuine. Second the product quality is protected, by discouraging opening of Dispensing Packs and exposure of vials and syringes of medicine to excessive heat and vibration as they are over-labeled or repackaged.

Therefore, Amgen supports the proposed key ideas listed under Section 4.1.3 and believes that any legislation should specifically prohibit repackaging, over-boxing and intrusive over-labeling of biological and other medicinal products.

Amgen Supports the Serialization of Sealed Packs of Biological Medicines according to Harmonized International Standards (Section 4.1.5)

Amgen endorses the ultimate adoption of a "sealed and serialized" approach to protecting biological medicines based on legally protected sealed outer packages that are serialized to ensure the source and authenticity of the packaged product.

Section 4.1.5 of the Consultation document seeks comments on mass serialization for pack-tracing and authenticity checks. Amgen believes that any EC legislation on this topic should harmonize internationally, especially with ongoing US efforts.

Specifically, the US Food and Drug Administration is also currently seeking input into the use of serialization to protect medicines.[3] Its authorizing legislation instructs the Agency to develop "numerical identifiers (which, to the extent practicable, shall be harmonized with the international consensus standards for such an identifier)."

[3] "Technologies for Prescription Drug Identification, Validation, Track and Trace, or Authentication; Request for Information," Docket No. FDA-2008-N-0121 (http://www.fda.gov/OHRMS/DOCKETS/98fr/E8-5599.htm); and "Standards for Standardized Numerical Identifiers, Validation, Track and Trace, and Authentication for Prescription Drugs; Request for Comments," Docket No. FDA-2008-N-0120 (http://www.fda.gov/OHRMS/DOCKETS/98fr/E8-5597.htm).

At present, the basic approaches being developed by the two jurisdictions are different:

- Europe appears more committed to pursuing an end-to-end authentication approach that involves manufacturers serializing individual packs, and pharmacies verifying the pack numbers at the point of dispensing;
- The US may be more committed to a full track and trace (or pedigree) model, where the manufacturer applies the unique serial number and the product chain of custody is verified and recorded at each step in its distribution.

Respecting these potential differences, we support strengthening product identification at the individual pack level through serialization of products using a unique identification number, established at the point of manufacture, contained within a standardized nonproprietary data format and architecture (e.g., according to the GS1 standards). To the maximum extent possible coding should be harmonized across the EU and also with the US and other counties, to optimize interoperability between regions.

General Comments in Support of Public Consultation

Broadly speaking Amgen supports the Commission's approach and the set of measures proposed to address the problems related to counterfeit medicines in Europe. We join in support of the comments filed by the European Federation of Pharmaceutical Industry Associations (EFPIA).

Amgen also agrees with the general concern of the Commission that "counterfeiters seem to veil the source of the product by selecting highly complicated distribution concepts." That would be an accurate description of the situation that surrounded the counterfeiting of Amgen product referred to above. Therefore, Amgen supports steps that decrease complexity and increase transparency and accountability within the distribution chain.

We would also like to stress that the proposed measures should be considered as a whole rather than individually or 'a la carte'. The proposed set of key ideas should be considered as part of a comprehensive strategy focused on ensuring that only the safest products reach the patient by strengthening the integrity of the supply chain and by adopting a number of additional, complementary measures in order to address the different aspects of this serious criminal activity.

Other controls the Commission should consider include the following: Increased Criminal sanctions, limiting sales of counterfeits over the internet and enhanced law enforcement.