# 2012

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June 8, 2012

The Honorable Tom Harkin Chairman Senate Committee on Health, Education, Labor, and Pensions 731 Hart Senate Office Building Washington, DC 20510

The Honorable Fred Upton Chairman House Energy and Commerce Committee 2183 Rayburn House Office Building Washington, DC 20515 The Honorable Mike Enzi Ranking Member Senate Committee on Health, Education, Labor, and Pensions 379A Senate Russell Office Building Washington, DC 20510

The Honorable Henry Waxman Ranking Member House Energy and Commerce Committee 2322A Rayburn House Office Building Washington, DC 20515

Re: Food and Drug Safety and Innovation Act of 2012 (S. 3187: Title X - Drug Shortages & H.R. 5651: Title IX - Drug Shortages) – Recommendations for Conference

Dear Chairman Harkin, Chairman Upton, Ranking Member Enzi and Ranking Member Waxman:

The American Society of Hematology (ASH) is supportive of your work to develop the Food and Drug Safety and Innovation Act of 2012 (S. 3187, H.R. 5651), particularly your efforts to begin to address the problem of shortages of drugs and biologics and would like to offer the following recommendations as you begin the work of the conference committee. The increasing problem of drug shortages has become a crisis taking a serious, sometimes life-threatening toll on hematology patients and negatively impacting the practice of hematology and the clinical research our members conduct. ASH thanks you for working in a bipartisan manner to pass this critical legislation by overwhelming majorities in both houses of Congress and commends you for including provisions to address shortages of drugs that are critical for hematology treatment and research.

ASH is the world's largest professional society concerned with the causes and treatment of blood disorders, representing more than 14,000 members who specialize in blood cancers such as leukemia, lymphoma, and myeloma, as well as serious blood diseases such as hemophilia. The country's shortage of more than 200 drugs has particularly affected ASH member hematologists and their patients because many of the drugs and biologics most vulnerable to shortages are used to treat blood disorders.

ASH supports many of the drug shortage provisions included in the legislation and believes this is a helpful first step toward ensuring that patients have access to the medications they need while not compromising safety and quality of those medications. The Society strongly supports the provisions regarding early notification, broad

parameters to define drugs in shortage, distribution of information about drug shortages to patient and provider organizations, and expedited review of manufacturing changes. However, the Society has the following recommendations to further strengthen the final legislation:

**Inclusion of Biological Products** – It is critical that manufacturers of all biologics and biosimilar products notify FDA of potential shortages. H.R. 5651 includes biological products within the definition for reporting, while S. 3187 leaves it up to the discretion of the Secretary. The Senate legislation specifically states: "The Secretary may by regulation apply this section to biological products (as defined in section 351 of the Public Health Service Act) if the Secretary determines such inclusion would benefit the public health." ASH urges you to include the language from the House bill that would require all prescription drugs, including biologics, be included in the early notification system and the other provisions in the drug shortage title of the PDUFA bill.

Inclusion of Products Derived from Human Plasma Proteins and Recombinant Products
Replacing Human Tissue - ASH is very concerned that products derived from human plasma proteins and recombinant products replacing human tissue – products used for the treatment of hemophilia and other bleeding disorders – are specifically exempted from the early reporting mandate in the legislation and urges you to remove this exemption from the legislation.

People with hemophilia and others dependent on plasma protein therapies and recombinant products have experienced the problem of drug shortages (Attachment #1 provides specific examples of national shortages of these types of products). Consequently, ASH strongly believes that there is no reason to exempt the products our community is dependent on from the requirement that manufacturers give 6 months advanced notification to the Secretary if they plan to interrupt or discontinue making a drug and they believe that it could result in a shortage of this drug.

While some manufacturers of plasma protein therapies and their recombinant analogs report production data to the FDA through a voluntary industry program the program does not include twenty plasma protein therapies and recombinant products for rarer bleeding disorders and Von Willebrand Disease. Moreover, not all manufacturers participate in the data collection program and neither the FDA nor the public is provided any information on a manufacturer's intent to stop or discontinue manufacturing of products, which could result in a shortage.

ASH believes that the reporting of production data is not a surrogate for advanced notification that a manufacturer intends to stop or interrupt production. FDA officials have informed the Society that the manufacturers' voluntary reporting of production data is very different from advanced notification of manufacturing changes and they did not see any reason to exempt plasma products and their recombinant analogs from the drug shortage reporting requirements.

ASH respectfully requests that you remove the exemption of plasma protein therapies and their recombinant analogs from the advanced notification requirement in the final legislation so that individuals with bleeding disorders and their physicians can appropriately plan for potential shortages of these life-saving products.

HHS Task Force and Strategic Plan – The drug shortages experienced over the past two years have revealed clear gaps in federal oversight and regulation. ASH supports the provision in the S. 3187 that directs the Secretary of HHS to establish a task force and to develop and implement a strategic plan to enhance the Department's response to preventing and mitigating drug shortages. Of particular note, the strategic plan required by the bill will include plans for effective communications with outside stakeholders and will consider the impact of drug shortages on research and clinical trials. ASH

strongly encourages you to include the provision to establish a task force and strategic plan in the final legislation.

Thank you for your attention to these important issues and your consideration of ASH's comments and recommendations. The Society hopes to continue to work with you as the bills are merged into final legislation in the coming weeks. Please contact ASH's Government Relations Manager Stephanie Kaplan (<u>skaplan@hematology.org</u> or 202-776-0544), if the Society can provide additional information or expertise.

Sincerely,

Armand Keating, MD President

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Attachment

# National Drug Shortages of Selected Biologic Products University of Utah Drug Information Service

Product	Shortage Dates	Comments
Albumin	1997	Coincided with IGIV shortage during 1997
	1/17/2006 - 10/19/09	Product was limited and allocated during
		this time. At some points the 5% solution
		was not available at all and centers had to
		dilute their own solution.
Anti-inhibitor Coagulant	5/4/2001 – 3/29/02	Essential treatment for some patients.
Complex products (Autoplex T,		Product was allocated or severely limited.
Feiba)		
ATGAM	9/24/2001 –	Interrupted transplant treatments
	11/27/2001	
Cytomegalovirus IG (Cytogam)	1/20/2006 - 9/19/2006	
	10/1/2007 - 5/27/2009	
Digibind	3/8/2011 - 09/07/2011	Antidote for digoxin toxicity, alternative
		was available, but it had different dosing
		and not all centers knew to access the
		product.
Digoxin Immune Fab	2/13/2008 - 5/2/2008	Antidote for digoxin toxicity, alternative
		was available, but it had different dosing
		and not all centers knew to access the
		product.
Factor VIII (Alphanate, Helixate,	5/5/2001 – 8/5/2002	Essential treatment for some patients.
Humate-P, Monclate P,		Product was allocated or severely limited.
Recombinate, Hemofil M,		
Kogenate, Koate, Refacto, Hyate		
Factor IX Products (AlphaNine,	5/4/01 – 8/5/02	Essential treatment for some patients.
Profilnine, Benefix, Mononine)		Product was allocated or severely limited.
Factor IX Complex (Bebulin)	6/10/2011 – 8/26/2011	Bebulin was unavailable, but Profilnine
		was available as an alternative.
Immune Globulin Products	1	
IGIV	1997	Severe shortage – required limiting and
		rationing therapy
	3/21/02 – 8/13/02	Gammimune only
	2005	Limited allocations of multiple products
	3/5/2011 – 05/17/2011	Gammagard only
	5/18/2012 – current	Gammagard only
Subcutaneous IG	3/25/2011 – 6/17/2011	Hizentra, Vivaglobin allocated, some sizes
		not available.
Gammastan	4/21/11 – current	Increased demand due to measles
		outbreaks

Prepared June 5, 2012 by Erin R. Fox, PharmD. Director, University of Utah Drug Information Service.