HFA
Hemophilia Federation of America™

NATIONAL HEMOPHILIA FOUNDATION
for all bleeding disorders

SAFETY SUMMIT

Impetus for Safety Summit

Safety incidents: 2019

- The bleeding disorders community experienced an unexpected number of recalls and other product safety notices in 2019.
- These events were unsettling to many:
  - They echoed tragedies of the recent past
  - They showed gaps in the system that serves the community in the present day
  - They highlighted a need to articulate standards that will serve the community as we enter into a new and uncharted era of gene therapy and other novel treatments.

HFA/NHF Response to Product Safety Issues

- Joint HFA-NHF communication at every step of the process with bleeding disorders community
- October 2019 letter to the community from HFA and NHF leadership
- Establishment of a shared inbox, “The Patient’s Voice,” to solicit community input on product safety concerns
- **Convening of a jointly-sponsored Safety Summit (Washington DC) in January 2020**

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Summit Mission

*"To articulate expectations for **monitoring, informing, educating, and communicating** issues related to product safety. To that end, we will identify the role that each stakeholder has in the process."*

Summit Participants

- Summit sought to have representation from every segment of the bleeding disorders landscape:
  - Patients
  - Patient organizations (state, national, and international)
  - Pharmaceutical manufacturers
  - Specialty pharmacy
  - Medical providers (physicians, nurses, HTC regional coordinators and directors)
  - Plasma Protein Therapeutics Association (PPTA) and the Patient Notification System (PNS)
  - Federal agency partners (HRSA, CDC, NIH)

Summit Framework

- Bring together stakeholders from diverse perspectives to discuss
  - Safety concerns and opportunities
  - How to improve communications channels / brainstorm best practices
  - The standards, rights, roles, and responsibilities of each stakeholder with regard to product safety
- Interactive format, with active participation from all attendees (mix of panel discussions and case study exercises)

Safety: *Current* Bleeding Disorders Landscape

Topics considered:

- Review of existing safety requirements, standards, and practices
    - How do these rules apply at different stages: during drug development, clinical trials, distribution of an approved drug, post-market assessment?
- How do different stakeholders **identify and define** safety in the hemophilia community?
- What are the expectations of different stakeholders with respect to monitoring, informing, and educating about safety-related issues?
- How do patients, families, and healthcare providers prefer to receive, act upon, and share safety notifications?

Current FDA Standards & Requirements

Manufacturers ***must***, and patients and providers ***may***, report the following events:

Safety Reporting in Clinical Trials

Sponsors must file an Investigational New Drug (IND) Safety Report when there is knowledge of a **suspected adverse, serious, or unexpected event**

Suspected Adverse Reaction

- Any adverse event for which there is a reasonable possibility that the drug cause adverse event
  - "Reasonable possibility" means a causal relationship between the drug and adverse event.

Serious

- Results in death, life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect (or requires intervention to prevent one of these outcomes)
  - In the view of the investigator or sponsor

Unexpected

- If not listed in investigator brochure
- Not consistent with the risk information described in the general investigational plan or elsewhere in the current application

Current FDA Standards & Requirements

A company can *choose* to recall a product or may be *requested or required* to do so by the FDA based on the following recall classifications:

Recalls

An action taken by a company to remove quantities of drug product from the market due to concerns about potential risks or hazards

Class I

- "reasonable probability" of serious adverse health consequences or death"

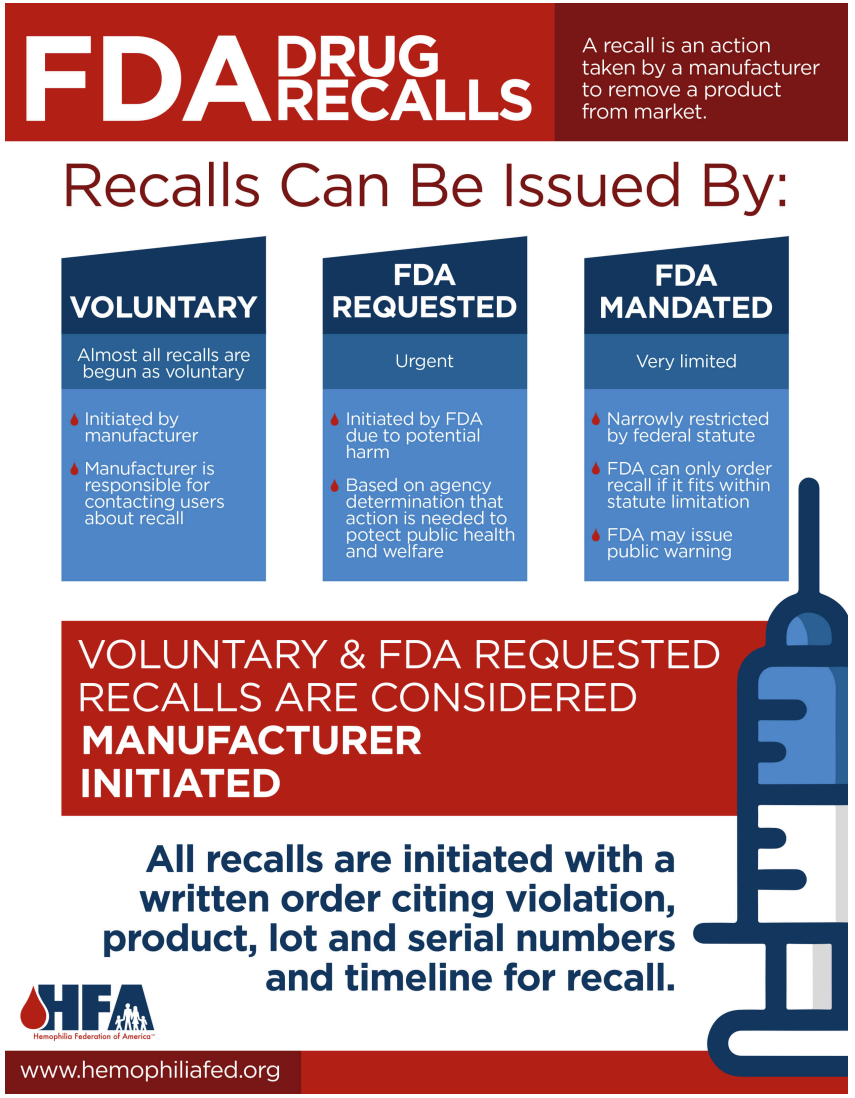
Class II

- "may cause temporary or medically reversible adverse health consequence" or "probability of serious adverse health consequences is remote"

Class III

- "not likely to cause adverse health consequences"

Understanding FDA Drug Recalls



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Safety Communications in the Current Treatment Landscape

- All stakeholders must re-educate themselves with the end goal of optimizing patient well-being.
- Patients are primary **sources** of information about potential safety events, as well as primary **recipients** of safety information. Determine how best to engage patients in safety reporting.
- Patients need clear, consistent, and concise messaging to come from trusted sources in a timely manner.
    - Stakeholders need to understand the role (complicating or otherwise) that social media plays in this process.
- Stakeholders should make effective use of the Patient Notification System (PNS, led by PPTA), which provides information to patients and health care providers on recalls and withdrawals of plasma-derived and recombinant therapies.

Safety Communications in the Coming Treatment Landscape: Gene & Novel Therapies

New treatment options may offer alternatives to the ongoing prophylactic or episodic use of medications with a limited half-life

- There will be unknowns about gene and novel treatments, such as efficacy, durability, side effects, etc.
  - What expectations do patients have around safety for these products?
  - Can single-use treatments be recalled after they have already been administered?
  - What post-marketing surveillance should happen nationally and internationally?
  - What are the differences for gene and novel therapies that impact notification about safety issues?
- To answer these and other questions, we will need ongoing patient monitoring and follow-up to include participation in national and international registries.
- **Current safety reporting practices should remain in effect.** Manufacturers, researchers, clinicians, and patient organizations must be transparent in communication whatever information is available, including any associated uncertainty. Patients, too, should recognize that they have a responsibility to keep open communication with their providers.

Consensus Principles

- All stakeholder must reaffirm commitment to **patient-centered communication**
- All stakeholders must have an awareness of **regulatory processes and roles**
- Patients are entitled to and should seek **trusted sources of information**
- The **patient perspective** on safety issues must be of primary importance
- Manufacturers, specialty pharmacies, health care providers, patient organizations, Patient Notification System and federal partners must have **defined communication strategies, protocols and outreach**
- Industry and federal partners must robustly adhere to **pharmacovigilance and recall procedures**
- All stakeholders must engage in **ongoing patient education**, including about clinical trials
- All stakeholders should **address gaps in data**, including through participation in registries and longitudinal studies

Safety Summit Key Takeaways

All Stakeholders

- Reaffirm commitment to patient-centered communication
- Recognize that regulatory requirements are the floor, not the ceiling
- Educate/self-educate on applicable standards, regulations, rights, roles, and responsibilities with regard to product safety
- Improve communications channels within and outside the bleeding disorders community
- Identify and define expectations for monitoring, informing, education, and communication of issues related to product safety
- Base actions on scientific data
- Leverage social media as appropriate/challenge social media in cases where incorrect or misleading information appears
- Be mindful of language used to describe novel and gene therapies
- International collaborations in safety communication and reporting will enhance consistency of messaging and completeness of reported data
- Develop checklist for reporting safety concerns and communicate their processes to other stakeholder groups

Safety Summit Key Takeaways

Patients

- Patients should educate themselves about
  - What is an adverse event and what other concerns to report to their provider
  - Basics of clinical trials, informed consent, drug safety reporting, novel therapies in pipeline
  - What are reliable sources of information
  - Understand that patients have a vital role as a source of safety information and in reporting issues to their medical provider
- Patients should track product lots
- Patients should enroll in PNS
- Patients should stay in communication with their health care provider
- Patients should understand the importance of participation in broad based registries to allow for information gathering and safety signal monitoring around existing and novel therapies

Safety Summit Key Takeaways

Patient Organizations

- Patient Organizations need to preserve and live up to their role as trusted sources of information
- Patient Organizations should identify designated staff for industry to contact in event of product recall
- Patient Organizations should have strategies in place to allow for prompt and accurate dissemination of product safety information via channels accessible to community members, in patient-friendly language, understanding that some patients may be off the grid and/or unconnected to HTC
- Patient Organizations should provide education about information sources and protocols including where should patients go for accurate news and information
- National Organizations should be aligned in their messaging
- National Organizations should promote strong ties and robust communications with state/local patient organizations
- Patient Organizations should promote enrollment in PNS
- Patient Organizations should offer foundational education to community members about clinical trials, safety reporting, etc.

Safety Summit Key Takeaways

Pharma (including sponsors of investigational drugs)

- Pharma should explicitly affirm and orient themselves with the end goal of optimizing patient well-being
  - Pharma should recognize that regulatory requirements are the minimum expectations of the bleeding disorders community
- Pharma should provide accurate, timely, and transparent guidance and information about safety issues to all stakeholder groups
  - Communications should be in patient-friendly language
  - Communications must be identifiable to manufacturer (e.g. on letterhead)
  - Communications must give clear guidance as to where and how recipients report adverse events, return product, etc.
  - Pharma should have direct communication with identified staff at national patient organizations
  - In the interest of timeliness, Pharma should publish safety information promptly, with the understanding that multiple communications may be required as further information develops
  - The presumption should be that the information contained in “Dear Healthcare Providers” letters are made public
- Pharma should participate in and make effective use of PNS
  - Pharma should activate PNS to communicate recalls
  - Pharma personnel should receive regular training about PNS and how to activate
- Pharma must provide long-term follow-up and support for recipients of novel therapies

Safety Summit Key Takeaways

Specialty Pharmacy Providers

- Specialty Pharmacy must recognize their critical role in receiving and disseminating safety information up and down the stakeholder channel
  - Specialty Pharmacy must make sure they get correct information
    - From Pharma, regarding any recall or safety event
    - From patient, regarding any suspected or reported adverse events
  - Specialty Pharmacy should reach out to patients, via channels optimized to patients, potentially including: text messaging, email, phone calls, postal mail, or other preferred communications technology.
    - When notifying patients about a recall, Specialty Pharmacy should also notify those patients' Health Care Providers, with the understanding that Specialty Pharmacy, not Health Care Providers, have the data linking individual patients to individual lot numbers
    - Specialty Pharmacy also should ensure delivery of replacement product to patients where applicable

Safety Summit Key Takeaways

Health Care Providers

- Health Care Providers should take patient safety concerns seriously and listen with empathy
- Health Care Providers should be a trusted source of information, providing patient friendly information and encouraging patients to ask questions
    - Health Care Providers should work with patients toward a shared understanding of what constitutes an adverse event
    - Health Care Providers should provide advance education to patients, e.g., about products still in pipeline
- Health Care Providers should stringently adhere to adverse event reporting requirements
- Health Care Providers should respond to manufacturer follow-up inquiries and make use of manufacturer Medical Science Liaison resources.
- Health Care Providers should promote enrollment in PNS, and potentially consider an opt-out system of patient enrollment rather than opt-in

Safety Summit Key Takeaways

Federal Partners

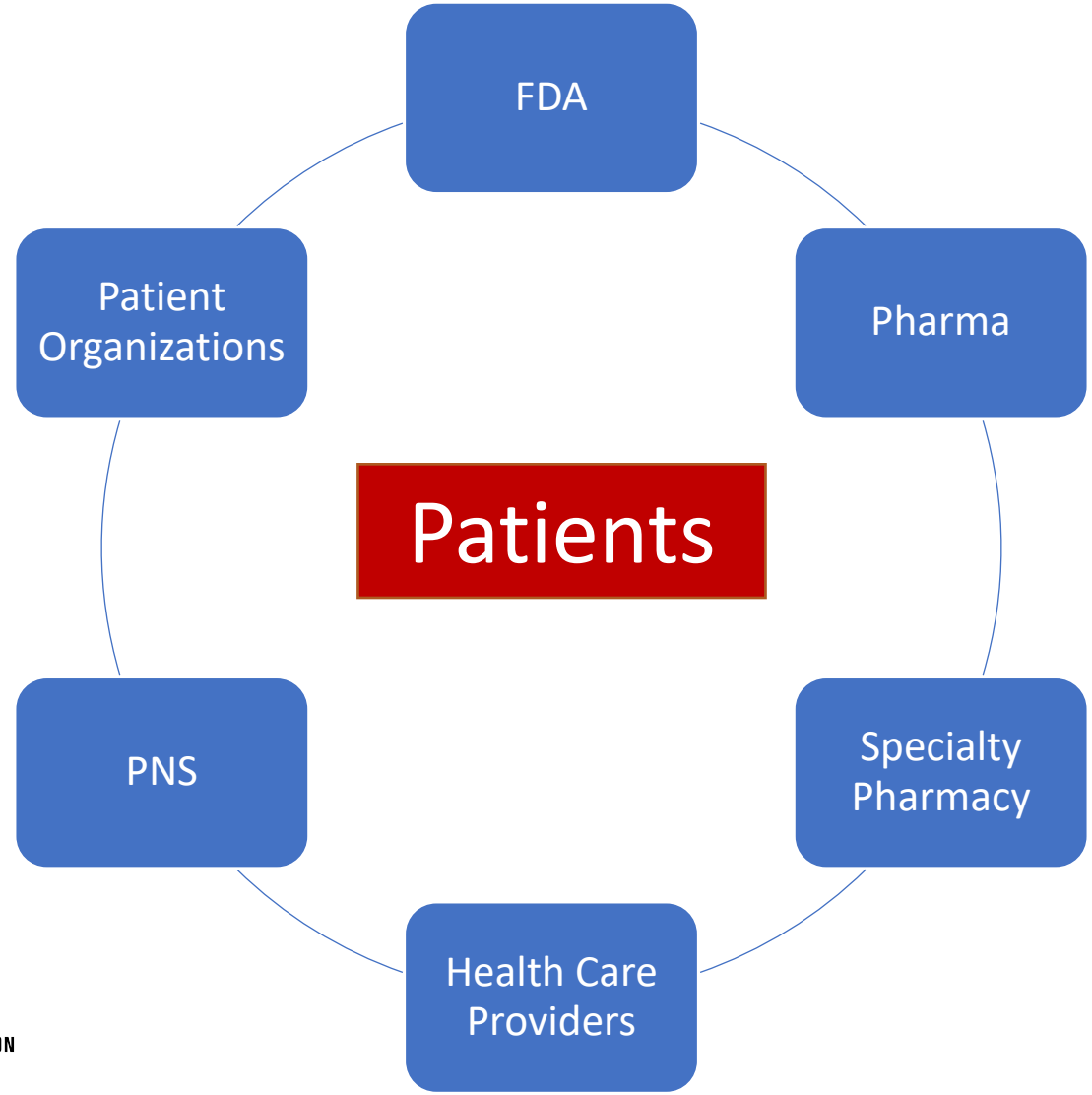
- Federal Partners should provide and require regulated entities to provide communications in patient-friendly language
- Federal Partners must ensure pharma compliance with post-market surveillance and reporting obligations
- Federal Partners should ensure that they and pharma provide good education regarding patient participation in clinical trials (before, during, and after the trials) regarding how to recognize and report potential adverse events or other safety concerns
- Federal Partners should encourage and support community surveillance initiatives

Safety Summit Key Takeaways

Patient Notification System (PNS)

- PNS should allow participation in PNS by manufacturers/sponsors of novel and gene therapies
- PNS should provide timely notifications in a range of formats and via a range of media that are self-tailored to individual recipients, understanding that some patients may be off the grid and/or unconnected to HTCs
- PNS should conduct regular tests to ensure that all stakeholders are engaged appropriately (on both ends: initiating and receiving notifications)

Patients are at the core of safety



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