

**FDA
BLOOD PRODUCTS ADVISORY COMMITTEE
MEETING**

**STATEMENT OF THOMAS L. MORAN
PRESIDENT, IDF**

**ON BEHALF OF:
IMMUNE DEFICIENCY FOUNDATION**

OCTOBER 5, 1999

Good Afternoon, I am Tom Moran, President of the Immune Deficiency Foundation. In numerous public forums the IDF has come forward on behalf of our community to discuss the serious shortage of IGIV in the US marketplace. As you have just heard from Dr. Winkelstein, primary immunodeficient patients, some 20 to 25,000 in the US, are dependent on regular infusions of IGIV to replace their incomplete immune system, and without IGIV suffer dire health consequences. The data and accompanying health effects we presented are the physician experience at a time when the IGIV market supply has slightly improved.

The IGIV shortage, which for our community began in December 1997 and persists today has caused significant increased illness and concern. These adverse health consequences we report to you today are caused by reduced supply. Indeed, if they had been caused by GMP related problems there would be a sensational outcry of concern from patients and the media, and stiff regulatory actions would occur. Instead, the governmental response to this experience has been muted and barely discernable.

According to the IPPIA data, from January 1, 1999 to June 30, 1999 - 7,848 kilograms of IGIV had been released for distribution to the US marketplace. If a projection can be made based on the first two quarters of 1999 we would assume that the US manufacturers would release a total supply of 15,696 kilograms in 1999. This assumption is based on the current production rate being maintained over the next two quarters. However at 15,696 kilograms of IGIV this is still a deficit of 1,300 kilograms from reported 1997 supply levels. 1997 is the last period when IDF estimated that supply of IGIV equaled demand. In addition, monthly IPPIA inventory data tells us that over the past 12 months, inventory has not exceeded a 15 day supply and in some months has been as low as a 9 day supply.

The FDA on various occasions has agreed that demand has not been met. The Agency has measured the shortage on occasion based on the number of emergency telephone calls they received requesting product. The Agency has announced that they have assigned a shortage officer to review supply and demand. IDF assumes that this action will allow for systematic review of activities the Agency can engage in which will increase supply in the marketplace. It becomes essential during this crisis that the Agency adequately track products in short supply and ensure that any action required be placed as a top priority. For instance, lot release.

Centeon was able to release lots of IGIV last week, marking their return to the marketplace. If Centeon can remain active for the balance of 1999 this will have a positive effect on the supply of IGIV. However, recent events have occurred which

cast doubt on whether the second half of 1999 will keep pace with the first half. The closure of Alpha Therapeutics for cGMP compliance problems last week, means that 285,000 grams of IGIV which are packaged and ready for release will not be allowed into the marketplace. Further, ZLB, manufacturer of two US licensed IGIV products, Sandoglobulin and Panglobulin recently announced a Panglobulin recall, initiated due to residual moisture in the final product container. The consumers are concerned that this problem will affect additional lots of Panglobulin and Sandoglobulin and limit near future output of IGIV from ZLB.

Based on this information the Immune Deficiency Foundation expects that the current rate of IGIV release in the US marketplace which projects to a total of 15,696 kilograms will not be sustained for the second half of 1999. The most troubling fact is that the supply in the first half of 1999 did not meet the demand for primary immune deficient patients, who are the beneficiaries of medical prioritization protocols. At the current rate, 46% of clinical immunologists treating over 25 patients are postponing infusions, 35% are increasing the intervals between infusions, 28% are reducing the dosages and 6% are employing alternative therapies. We would assert that such strategies are valid surrogates for adverse health effects within our communities. The public health consequences of those adjustments should be reviewed and understood in order to develop appropriate public policy responses.

The IDF makes the following recommendations to this Committee:

1. The aggregate industry data should include supply projections for IGIV two quarters in advance, and continue to supply retrospective inventory data.
2. The industry should continue its commitment to supporting emergency supply programs, like the IDF's Safety Net Program and promote rationing protocols.
3. The health consequences at the current level of supply should be evaluated. A national health surveillance program monitoring the experience of immune deficient patients would answer questions regarding the impact of reduced supply.
4. The FDA should expedite approval of new applications for licensure and processes and promote research into establishing surrogate end-points with the National Institutes of Health.
5. Strategies should be employed to distribute non-US licensed IGIV product on an emergency basis for companies involved in safety and efficacy studies.

There are programs designed to address equitable distribution of available supply, such as each manufacturers emergency supply program, the IDF Safety Net Program and the promotion and adoption of prioritization protocols within major medical centers. Yet in spite of rationing protocols, and when available the use of alternative

therapies, short and long-term management of available supply has helped, but not solved the problem. As evidenced by the IDF physician survey data.

Critical issues involving the US IGIV manufactures' compliance with current cGMP, increasing importation of offshore IGIV and expediting new applications for IGIV licensure and processes must be addressed as solutions to the current supply shortage.

I would like to address these issues beginning with the cGMP. As a patient advocacy organization, the safety of the blood supply has been our top priority. The experience of our population, representing long term recipients of plasma derived therapeutics is one of an almost completely unblemished safety record. Conversely, our data and Dr. Winkelstein's testimony demonstrates that many individuals have become gravely ill as the result of availability. Plainly stated, if manufacturers continue to produce at reduced capacity patients suffer.

Secondly, I would like to address the importation of IGIV from offshore manufacturers. The IDF met with the FDA at the request of our medical community who was astonished by clinical trial requirements, believing that a number of the end-points required by the Agency meant hardship for patients who would have to undergo extensive blood draws and intrusive diagnostic tests. A scientific forum was created in March of 1999 to address clinical trial design and requirements, which the FDA participated in. The IDF medical community believes that these products are bioequivalent, and that clinical trial requirements should include safety and pharmacokinetic studies only. The Agency has not been convinced on this point although they have discussed with IDF reducing the number of patients currently required in clinical trails and agreed to a study which would include safety, pharmacokinetics and therapeutic non-inferiority concurrently. Further, the Agency has agreed that a trial conducted over a twelve month period would be adequate for licensure.

I would like to note that the trial I have just described to you is much more extensive then the original trials conducted on the six brands that are currently licensed in the US. IDF has agreed to assist one European manufacturer and is in active discussion with three additional manufacturers, two of whom are currently conducting business in the US, to develop clinical trial protocol and submit an IND. IDF will assist in clinical site and patient recruitment, in an attempt to further assist our patients in obtaining an adequate supply of product. We are at a critical moment, one year ago there was a similar level of interest which was quickly squashed by the unnecessary clinical trial requirements. The IDF approach, developed with FDA cooperation, has renewed the interest of manufacturers to the extent that several are willing to invest

the associated costs. This is a viable long-term solution. There is safe, available product off shore which should be expedited into the US to assist in this crisis.

Another solution is immunoglobulin which is produced off shore and could be administered by an alternative route. These non IV products will require the Agency to be cooperative when designing studies which compare them to IGIV products. The safety and efficacy of immunoglobulin as well as supply should not be moved from the forefront of these discussions. The world wide fractionation industry is attempting to assist the US and solve this shortage. Manufacturers should not be blocked from doing so by raising the bar in the name of scientific research at a time when lives are at stake.

To conclude IDF recommends that collaborative efforts be undertaken. If we can engage the cooperation of key groups, we might be able to accomplish these tasks in an efficient, timely manner to ensure that patients who do not have medically equivalent therapies are able to obtain the life sustaining medications on which they are dependent.

Thank you. I would be happy to answer any questions.

TO:	Jerry Winkelstein
FROM:	Miriam O'Day
DATE:	August 23, 1999
RE:	HHS Testimony

Medical elaboration on the following:

- ✓ Data from the IDF Physician shortage
 - Two key factors to consider:
 - Immune deficient patients are the beneficiaries of medical prioritization
 - Market supply is slightly increased over previous periods surveyed

- ✓ Implications for patients not receiving optimal care
 - The shortage is current critical and ongoing
 - We can not guarantee enough IGIV for our patients
 - Prioritization protocols and distribution strategies have not been 100% successful
 - We have switched brands, increased intervals, decreased dosage and employed alternative treatment strategies in a fragile and dependent patient population
 - People are getting sick