Seventeenth Meeting of the Secretary’s Advisory Committee on Heritable Disorders in Newborns and Children  
Testimony of the Immune Deficiency Foundation  
Marcia Boyle, President  
February 26, 2009

I want to thank the Secretary’s Advisory Committee on Heritable Disorders in Newborns and Children for giving me the opportunity to comment in favor of adding Severe Combined Immune Deficiency (SCID) to newborn screening panels.

Founded in 1980, the Immune Deficiency Foundation (IDF) is the national patient organization dedicated to improving the diagnosis, treatment and quality of life of persons with primary immunodeficiency diseases through advocacy, education and research.

The federal government conducts the National Health Interview Survey, the National Health and Nutrition Examination Survey and funds the Behavioral Risk Factor Surveillance Surveys to better understand the incidence and prevalence of common acute and chronic conditions in the population. Less common medical conditions, like primary immunodeficiency diseases, are not tracked in these studies. Consequently, as part of its mission to improve the health of persons with these conditions IDF conducts surveys to better understand these diseases, their treatment and the outcomes. Because of the unique problems of our SCID families, IDF initiated a special survey of these families to understand their experiences with diagnosis and treatment. We developed a national sample of 208 families identified as having a family member with SCID from the IDF database, the SCID forum database, and the SCID Angels for Life database. The survey was conducted as a self-administered interview by Web and mail between January 13 and January 30, 2009. Despite such a brief field period, with only one email and one email reminder, and one regular mailing, we achieved a 63.5% response rate, with 124 eligible families with a total of 156 SCID cases in those households as the basis
for this analysis. (Figure 1). This data is preliminary, as more responses came in after the cut off period for this analysis.

Findings:

In households with any SCID cases, 80% of families reported one diagnosed child, 15% reported 2 children, and 6% reported 3 children, for a total of 156 SCID cases. **Of this group, 59 children, or 38% have died. This is a true tragedy, since we know SCID is curable if diagnosed and treated early. Indeed, 30% of these children were not diagnosed until after they died. If we had newborn screening, these children could be alive today.** (Figure 2)

The data that follows is based on the respondents answering about their oldest surviving child with SCID, or if none have survived, the oldest deceased child. Out of these 124 cases, 20 were tested at birth due to a family history of SCID, and therefore were spared becoming infected prior to diagnosis. A total of 104 parents of SCID patients not tested at birth were asked about the time of symptom onset vs. time of diagnosis for those children. The survey demonstrates the early onset of SCID symptoms with a mean age of **11.3 weeks** and a median age of **8 weeks at symptom onset.** Age at diagnosis, sadly, is much later than symptom onset for those not diagnosed at birth with a mean age at diagnosis of 26.1 weeks and a median age of 24 weeks. **The age of diagnosis is three times the age at symptom onset.** As medical literature points out, with SCID children, it’s important to avoid the opportunistic infections that can severely disable or kill them. The current average delay in diagnosis after symptom onset is the difference between life and death. Newborn screening and the early initiation of treatment could prevent most SCID children having such infections. (Figure 3)

Not surprisingly, 90% of children had to go to a major medical center for diagnosis, with only 5% at a physician’s office. 80% of cases were diagnosed in the same city or state where they live. (Figures 4, 5)

**Nearly nine out of ten SCID children (89%) received definitive treatment for the condition.** Of the treatments reported, 95% were bone marrow transplant, 2% were gene therapy, and 11% were Peg-ADA. Nearly half (45%) of patients were treated in the same city or state in which they live. (Figure 6)

Only thirteen children (11%) never received treatment for the condition. Of these, 85% had died (62%) or had become too ill (23%) to receive treatment. **No one reported that a child was not treated because treatment was not affordable or available. It is late diagnosis, not the cost or availability of treatment, which is the barrier to care for these children.** (Figure 7)

According to the article published in the New England Journal of Medicine, Feb. 18, 1999, “Hematopoietic Stem-Cell Transplantation for the Treatment of
Severe Combined Immunodeficiency,” authored by Dr. Rebecca Buckley, et al, if a bone marrow or stem cell transplant occurred before 3.5 months of age, 95% of SCID infants in their series at Duke University survived, as compared to only 76% who were treated when they were 3.5 months or older. Updated data from the Duke University Medical Center shows a 96% survival rate for 48 SCID infants treated in the first 3.5 months of life, and a 66% survival rate for infants treated after 3.5 months. (Figure 8)

In our survey, only 23.7% of patients were treated by 3.5 months, 50% were treated by 6.5 months, and 75% were treated by 9.2 months. Consequently, the vast majority of SCID cases in our survey received treatment significantly later than the period of 3.5 months quoted by Dr. Buckley. Those in our survey who were diagnosed early and treated by 3.5 months had a 91% survival rate. Those treated after 3.5 months, had a 76% survival rate. Thus the findings from our survey of 109 treated SCID cases mirror those of Dr. Buckley’s study. (Figure 9). (Although a small sample, this is significant at the 90% confidence level)

Of our respondents who had a SCID child who received treatment, 79% reported that the child was still living, and 21% reported the child is deceased. 82% of those still alive (mean age of 8.6 years) report that they currently see a specialist for SCID. Over half of these children don’t need to visit a transplant specialist more than every 6 to 12 months, with 11% reporting every 2 years. (Figures 10, 11).

Very importantly, the average age at treatment in weeks was 29 weeks for those who are alive, and 58 weeks for those who are deceased. As you can see, this is significant at the 95% confidence level. (Figure 12)

Conclusions:

Without treatment, Severe Combined Immune Deficiency Diseases are fatal, because those with the condition have no protection from the infectious agents that surround us. These viruses and bacteria, for which the rest of us have natural immunities, produce uncontrolled infections in SCID children. This survey demonstrates that timely diagnosis and treatment makes the difference between life and death for these children. Moreover, the survey demonstrates that very early diagnosis and treatment is the real key to survival, but without newborn screening this is not available for the great majority who lack a family history. If disease is recognized only as a result of infection, it is often too late for effective treatment. Hence, screening at birth can mean the difference in a life measured in many years, rather than in weeks. Given this data, it would be inconceivable to me that the committee would not vote in favor of adding SCID to the Newborn Screening panel. Thank you again for your interest and time. And thank you for a vote to save lives and unnecessary suffering.
Figure 1
Number of Diagnosed SCID Cases in Each Household

- 124 Households
- 156 cases of SCID
- 64% response rate

Q2a. How many people have ever been diagnosed with SCID in your household? (N=156)

Source: 2009 IDF SCID Survey
Q2b. How many if any have died? (N=156)

- 59 total reported deaths
- 38% of all cases resulted in the death of a child
### Figure 3

**SCID Symptom Onset & Age of Person in Weeks at Diagnosis**

<table>
<thead>
<tr>
<th>Age of Symptom Onset</th>
<th>Age at Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean: 11.3</td>
<td>Mean: 26.2</td>
</tr>
<tr>
<td>Median: 8.0</td>
<td>Median: 24.0</td>
</tr>
</tbody>
</table>

- 25% diagnosed by 3.2 months
- 50% diagnosed by 5.5 months
- 75% diagnosed by 7.4 months

Q2e_1. At what age (in weeks) did the person first start having symptoms of SCID? Base: Those not tested at birth due to family medical history (N=104)

Source: 2009 IDF SCID Survey
Q7a. Was the patient diagnosed at a medical center or at a physicians office? (N=124) Base: oldest surviving child with SCID/ oldest deceased if no surviving SCID

Source: 2009 IDF SCID Survey
Figure 5
Travel for Diagnosis

Source: 2009 IDF SCID Survey
Figure 6

Travel for Treatment

Source: 2009 IDF SCID Survey
Q8b. What was the main reason the person did not receive treatment? (N=13) Base: Those diagnosed but not treated

Source: 2009 IDF SCID Survey
Hematopoietic Stem-Cell Transplantation for the Treatment of Severe Combined Immunodeficiency

Rebecca H. Buckley, M.D., Sherrie E. Schiff, B.S., Richard I. Schiff, M.D., Ph.D., M. Louise Markert, M.D., Ph.D., Larry W. Williams, M.D., Joseph L. Roberts, M.D., Ph.D., Laurie A. Myers, M.D., and Frances E. Ward, Ph.D.

“Of the 22 infants who received transplants before they were 3.5 months old, 21 (95 percent) survived, as compared with 51 of 67 (76 percent) who received transplants when they were 3.5 months or older (P=0.088).”

*Updated data from Duke University Medical Center:
(A) - 48 SCID infants treated in first 3.5 months of life: 96% survive
(B) - 113 SCID infants treated AFTER 3.5 months of life: 66% survive

* Kaplan-Meier Plots reprinted from: J ALLERGY CLIN IMMUNOL 2007; 120 (4): 760-768, Population-based newborn screening for severe combined immunodeficiency: Steps toward implementation, Jennifer M. Puck, MD
# Figure 9

## Treatment in Months by Mortality: 2009 IDF SCID Survey

**IDF 2008 National Survey of Severe Combined Immunodeficiency**

<table>
<thead>
<tr>
<th></th>
<th>Mortality</th>
<th>Total</th>
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<tr>
<td></td>
<td>Deceased</td>
<td>Alive</td>
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<tr>
<td><strong>Treated by 3.5 months</strong></td>
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<td></td>
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<tr>
<td>Count</td>
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<tr>
<td>%</td>
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<td><strong>Treated after 3.5 months</strong></td>
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</tr>
<tr>
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<tr>
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</tr>
<tr>
<td>%</td>
<td>21.1%</td>
<td>78.9%</td>
</tr>
</tbody>
</table>

P = .08, Fisher’s exact test

Source: 2009 IDF SCID Survey
Q14. Does the patient currently see any type of specialist specifically for SCID?: Base: Those reporting treatment (N=86)
Q16. How often does the person visit the transplant specialist?: Base: Those reporting they see specialist (N=67)

Source: 2009 IDF SCID Survey
Figure 12
Average Age at Treatment in Weeks by Mortality*

Q11. What was the person’s age at the time of treatment?, Q13a. Is this person deceased? Base: All who reported treatment (N= 97)

*P = .038

Source: 2009 IDF SCID Survey,