I. Introduction and Background

Most experts agree that the incidence of pediatric neurological dysfunctions (e.g., autism, ADD/ADHD, CFIDS) has increased at least four to five times in the last decade, a disturbing trend that deserves national attention. In addition, the vast majority of emerging evidence connects this trend to the dysfunctional inter-relationship of the neurological and immune systems. However, most of the existing organizational efforts to date have focused on identifying the specific etiology of these dysfunctions prior to developing treatment options. While etiology is a critical aspect of any search for a cure, it is also critical that potentially effective therapies be concurrently pursued to maximize the potential of these populations. History tells us that the pursuit of an etiology (or more likely etiologies for these populations) through the standard academic research mechanisms may take at least seven to ten years to derive results. Moreover, these results may only provide indirect leads to treatment options, leads that require further time and research before these children can be helped.

The Neuro-Immune Dysfunction Syndrome (NIDS) Medical Advisory Board believes that this extended timeline will likely minimize the chances for this generation of NIDS children to join mainstream society. Pre-adolescent children with a NIDS related disorder cannot wait seven to ten years for a treatment hypothesis to be formulated based upon research related to etiology. ***Thus, the NIDS Board will focus all of its energies on the identification of NIDS pathologies and related treatment options and seek to make them available to this generation of children.***

The NIDS Board has decided to take this aggressive research approach because it believes that children with NIDS can fully recover with the appropriate interventions. ***The fundamental premise of the Board's clinical hypothesis is that children with NIDS have dysfunctional, not permanently damaged, neurological systems.*** With this clinical hypothesis in place, the Board believes it has no choice but to expedite treatment research in order to save thousands of NIDS children from a lower than necessary quality of life.

However, the NIDS Board also believes that any clinical treatment options that it identifies will not provide a fail-safe "cure" for NIDS patients. The medical treatments must be supplemented with the appropriate rehabilitative and educational interventions, as many of these children have missed years of development based upon their neurological dysfunction. Thus, the Board will aggressively pursue a three-tiered approach to NIDS recovery:

I. Introduction and Background (continued)

Step One – Return the child's brain to a functional state through appropriate medical interventions

Step Two – Rehabilitate the child through intensive cognitive rehabilitation therapy with rehabilitation professionals

Step Three – Educate the child socially and academically through controlled integration efforts in the public school system

This approach will require the cooperation and coordination of the medical and educational systems, a cooperation that does not exist today. The Board will attempt to maximize the relationship of

these two systems through the focused education of medical and educational professionals regarding the treatment/therapy options the children need and the positive impact the delivery of these treatments and services can have on the prognosis for these children. It should also be noted that millions of dollars in custodial care and other support modalities can be saved if we intervene today and avoid the need for costly services that do little to improve the quality of a child or adult's life.

The following business plan considerations have been developed to assist the Board with its mission of reaching out to NIDS children TODAY, not in ten years. ***The Board believes that this generation of NIDS children can be saved with some solid planning and the right sense of urgency!***

II. Mission Statement

The NIDS Medical Advisory Board exists to expeditiously facilitate access to new clinical and pharmaceutical therapies for children with Neuro-Immune Dysfunction Syndromes (including autism/PDD, ADHD, and CFS/CFIDS) as well as to increase the public's awareness of the potentially optimistic prognosis for NIDS children if they are offered the appropriate medical, rehabilitative and educational interventions in a coordinated fashion.

The NIDS Advisory Board is also committed to utilizing only those research and evaluation mechanisms that emphasize objective and scientific principles and preserve the best interests and safety of the patients and families it serves.

III. Goals and Objectives

The Trustees of the NIDS Medical Advisory Board have adopted a primary objective of **providing NIDS patients and their families with additional clinical therapy options in 2000**. In order to meet this primary objective, the Board has also adopted the following additional goals and objectives:

- To focus on the **pathology and treatment** of NIDS related disorders, not necessarily the etiology of such disorders

- To further explore the **neuro-immune inter-relationship** and its role in the manifestation of NIDS related symptoms

- To integrate and maximize the professional expertise necessary to **comprehensively address the pathology of NIDS.** This will done through the on-going national expansion of the Board to include:

    - Primary care pediatrics
    - Pediatric neurology
    - Pediatric immunology
    - Pediatric rheumatology
    - Pediatric endocrinology
    - Pediatric rehabilitation

- To **develop homogeneous sub-groups of NIDS patients** through immune profiling techniques to facilitate the application of appropriate clinical and pharmaceutical therapies

- To secure private and public funding for clinical trials of pharmaceutical agents through the education of the private and public sectors **utilizing objective and scientific data** (e.g., Brain SPECT scan analyses, immune system profiling)

- To develop NIDS diagnoses criteria to facilitate the identification of these populations based upon medical markers in lieu of behavioral symptoms

- To develop strategic alliances with interested health care participants such as pharmaceutical companies, academic research institutes, private practitioners, and patients **to form a clinical therapy "pipeline" for new and innovative therapies for NIDS patients**

III. Goals and Objectives (continued)

- To begin to educate the general public with regard to the emerging understanding of NIDS pathology and **the potentially optimistic prognosis for NIDS patients**

- To begin to integrate medical and educational needs of NIDS patients through the **development of a comprehensive medical/educational model of treatment**

IV. Environmental Assessment

The following environmental assessment was conducted to confirm the viability of the NIDS initiative and whether the pharmaceutical industry will have a strong interest.

Empirical Evidence

NIDS and MAT commissioned and completed a review of United States Department of Education classification data and CACI demographic data relative to the national trends in special education and general population growth. The following trends were identified:

- Although the general school age population (ages 5-19) is projected to grow approximately 10.5% between 1991-92 and 2000-2001 (to 59.7 million children), the special education population is projected to grow by over 30%! This includes classifications such as Autism, Specific Learning Disabilities, Speech and Language Disorders, Multiple Handicaps, Emotional Disturbances and Mental Retardation. The fastest growing classifications during the time period reviewed are Autism (a 1000% increase), Specific Learning Disabilities (a 34.5% increase) and "Other Impairments" (a 500% increase). The latter category includes the Attention Deficit Disorder (ADD) population.

- This means that almost 10% (5.7 million) of children in the United States will be classified in one of these categories as we begin the new millenium, with 1.3 million of those children having been added during the ten year projection period! It should also be noted that these projections are highly conservative and based upon historical data which we know through anecdotal information understates the problem. Once we can obtain actual data for the last four years of our review period, we are likely to find an even larger problem that will only worsen without coordinated intervention from the medical and education communities.

This data reinforces the magnitude of the NIDS epidemic and confirms that the target population is large enough to gain the support of the pharmaceutical industry. The latter observation is based upon the fact that even if the NIDS initiative only targets 10% of the special needs population in 2001, it represents 570,000 potential users of immune modulating agents. If these agents retail (on average) $175 per month, the initiative produces a revenue stream of over one billion dollars annually, a minimum objective for pharmaceutical companies.

Other Disease Incidence Rates (in order of magnitude)

Disease	**Incidence Rates**
• Autism	20 to 40 per 10,000 (NIH/CDC estimate)
• Cystic Fibrosis	TBD
• Multiple Sclerosis	TBD
• Down's Syndrome	TBD
• Alzheimer's Disease	TBD
• ALS	TBD

Other Disease Category Funding Rates (in order of funding rates)

Disease	**Funding Rates (per individual)**
• ALS	TBD
• Cystic Fibrosis	TBD
• Multiple Sclerosis	TBD
• Downs Syndrome	TBD
• Alzheimer's Disease	TBD
• Autism	Less than $20 per autistic individual

It should be noted that each of the other disease categories noted above enjoy significantly greater research funding than autism despite lower incidence rates. The NIDS initiative will attempt to

modify this current disparity in research funding.

Anecdotal Evidence

Rehabilitation Center Survey

An informal survey of rehabilitation centers in the Northeast that serve children with autism indicates that referrals have increased at least ten fold in the last two years. Specific results are available upon request.

Pharmaceutical Industry Interviews

The following pharmaceutical companies have interviewed by NIDS (and MAT) personnel:

- Glaxo Wellcome
- Bristol Myers Squibb
- Smith Kline
- Roche Laboratories

The feedback from these sessions can be summarized as follows:

- Autism remains categorized in the same "clinical" area as schizophrenia and other behavioral health disorders
- Children are considered high-risk subjects for trials primarily based upon their immature immune systems and the need for parental approval
- A minimum revenue threshold for a given project is approximately one billion dollars in annual sales
- "Fast track" efforts are gaining acceptance where grass roots efforts are strong and gain the public's attention (e.g., the Alzheimer's fast track process by Bristol Myers Squibb)
- According to a survey sponsored by the Pharmaceutical Research and Manufacturers of America, 95 pharmaceutical and biotechnology companies are developing medicines for children
- The same survey also found that 20 new medicines for pediatric disorders were developed and approved last year. 187 additional medicines are either undergoing testing or awaiting FDA approval, including:
    - 44 for cancer
    - 14 for cystic fibrosis
    - 13 for asthma
    - 12 for AIDS
    - 9 for epilepsy (which affects 600,000 children)
    - 3 for rheumatoid arthritis (which affects 50,000 children)

In contract, only one (1) "medicine", secretin, is being tested for the indication of autism despite the fact that an estimated 300,000 children are affected based upon estimates that one of every 500 births since the mid-1990s develops a form of autism.

V. Clinical Hypothesis

Please refer to the attached Clinical Hypothesis Statement and immune profiling description for the a review of the clinical aspects of this business plan. In addition, an analysis of the existing NeuroSpect data (over 100 scans of autistic children) is underway and should be completed during the fall, 1999.

VI. Organizational Structure

The composition of the Board of Directors and the organizational by-laws are enclosed as Exhibits III and IV. The primary objective of the Board composition is to integrate the professional expertise of multiple medical specialties to adequately address the mission of the Board. In addition, management support is currently being offered by Medicine for Autism Today (MAT), a non-profit organization developed to support research organizations focused on treatment options for autism. The MAT Board includes several health care professionals who are qualified to provide management support to an initiative such as this one.

In addition, the narrative below outlines how NIDS may relate to MAT and the Orphan Drug Development (ODD) initiative, an organization that is likely to assist NIDS in meeting its goals and objectives.

Mission Statements

MAT – To aid in the development of a cure (and short-term treatment options) for autism through the funding of relevant research efforts (including NIDS research) and the provision of management support to initiatives focused on autism treatments

NIDS – To facilitate the development of treatment options for NIDS disorders including autism, chronic fatigue syndrome, ADD, lupus, MS, ALS, etc.

ODD – To evaluate the effectiveness of existing immune modulating agents (approved for other indications) on NIDS related conditions

Proposed Inter-relationship:

MAT is a parent-driven "foundation" that evaluates funding requests from any source, including NIDS and ODD, and financially and administratively supports those requests that relate to autism clinical profiling and/or trials.

Board composition is parents of children with autism and other NIDS related conditions and appropriate business personnel to assist research organizations, including NIDS and ODD, as necessary with implementation work.

VI. Organizational Structure (continued)

Fund-raising targets include private foundations, other parent support groups, general solicitations (e.g., NYC marathon, dinner dances, etc.)

NIDS is a medical advisory group focused on the development of clinical protocols and the coordination of clinical trials for NIDS conditions. Its primary funding sources will be any parent support group interested in the NIDS movement (including MAT, CFIDS Association, MS Society of America, etc.) and the pharmaceutical/biotech industry.

The board composition is limited to clinicians focused on NIDS research and treatment options, with autism being represented by multiple seats (number to be determined).

ODD is a for-profit business venture dedicated to the re-deployment of existing medications for use in NIDS treatment. Funding sources will include private foundations (i.e., the Estee Lauder and

Alzheimer's Foundations), parent support groups, the biotech industry and the pharmaceutical industry.

ODD's board composition will include senior pharmaceutical and biotech executives as well as clinicians interested in NIDS research.

NOTE: MAT could fund projects for NIDS and ODD or provide funds to NIDS for disposition to ODD. Of course, MAT can restrict these "grants" to focused areas of utilization (i.e., clinical trials for autistic children) or permit more general use of the funds (e.g., NIDS research)

Fast-Track Clinical Trials Pipeline

1. ODD purchases the sub-license for a given agent that may have application in NIDS-related conditions (e.g., Peptide T and VIP)

2. ODD asks NIDS to develop protocols and profiles to target a given population for a clinical trial

3. MAT provides funding and management support to NIDS to facilitate profiling and trials

This "orphan drug pipeline" is a critical success factor for helping this generation of children because the lengthy development of new agents is omitted from the process.

VII. Strategic Workplan: PROJECT 2000

In order to explore, evaluate and confirm its central hypothesis and meet its goals and objectives, the NIDS Medical Advisory Board will follow the following four step strategic workplan:

Development of the Fast-Track Clinical Trials Pipeline

1. ODD must be incorporated and board development must include some members of the NIDS Board
2. ODD purchases the sub-license for a given agent that may have application in NIDS-related conditions (e.g., Peptide T and VIP)
3. ODD asks NIDS to develop protocols and profiles to target a given population for a clinical trial
4. MAT provides funding and management support to NIDS to facilitate profiling and trials

Development of NIDS sub-groups

Based upon the hypothesis that multiple etiologies/pathologies exist within the spectrum of NIDS disorders, the Board will first seek to develop homogeneous sub-groups to facilitate the development of treatment options. In order to accomplish this goal, the Board is currently in the process of developing a clinical profile/protocol based upon the clinical review of 100 or more normal subjects (no exclusion criteria necessary) and 200 NIDS subjects (three to five years of age with minimal medication history). The review will be done at two locations: the University of Miami (where cytokine "proxies" will be measured) and a location equipped with a Becton-Dickinson cytokine analyzer. The Board's preliminary assessment indicates that at least four NIDS sub-groups may be identified.

Funding required: $50,000 (assistance with lab fees)
$50,000 (leasing fees for B-D analyzer)

Facilitation of Animal Trials

Animal trials may be necessary to evaluate agent safety and potential effectiveness prior to human trials.

Funding Required: $150,000

NeuroSpect Analysis and Network Development

An analysis of existing NeuroSpect data is underway to determine its utility in this process. At present, subjects involved in the immune profiling do not require a NeuroSpect scan (either prior to or after treatment). However, during the clinical trials, scans will be required prior to and after experimental treatment. In order to standardize the diagnostic aspects of this analysis, at least three (3) sites will be electronically integrated and provided with initial research funds (e.g., $50,000 per site)

Funding Required: $100,000 (network integration costs)
$150,000 ($50,000 per site for research funding)

Integration of the pharmaceutical industry

Based upon the analysis of the above data, the Board will identify the most appropriate potential clinical therapies available for each sub-group and approach the pharmaceutical industry, potentially through ODD to participate and fund clinical trials. The fundamental tenet of this effort will be to convince several pharmaceutical companies that the identification of effective treatments for NIDS patients (utilizing existing agents) will offer them tremendous marketing and financial advantages by being part of an effort to save thousands of children from a low quality, non-productive life. The pharmaceutical companies will also be saving the costs associated with new agent development.

Funding Required: $25,000 (costs associated with presentations to key pharmaceutical contacts)
$50,000 (general operating expenses)

Clinical trials

The NIDS Board, in conjunction with ODD, select academic sites and the appropriate pharmaceutical companies, will conduct clinical trials in accordance with industry standards to ascertain the efficacy of select pharmaceutical agents in the treatment of NIDS related disorders in children. In addition to Brain SPECT analyses, careful pre- and post-trial functional analyses will be conducted to ensure that functional improvements and positive outcomes in the children are measured objectively.

Funding Required: $175,000 (for the agent costs and lab fees associated with a trial on autistic children)

It should also be noted that NIDS is currently pursuing funding for a clinical/research fellowship through a private foundation to assist with the clinical aspects of the immune profiling and the clinical trials.

VIII. Marketing Plan

NIDS is in the process of retaining a consultant to develop a marketing plan that will available in the Fall, 1999 under separate cover. However, the NIDS Board has agreed that the primary theme of the marketing plan will be to expose NIDS as a disease process of epidemic proportions.

IX. Financial Considerations

The NIDS Advisory Board is a 501©(3) not-for-profit corporation in the state of California. Its primary source of revenue support prior to formal clinical trials will be through targeted fund-raising efforts. A formal fund-raising plan is under development and will be shared as soon as it is available. For purposes of this business plan document, which projects a funding need of $750,000, the Board will be targeting the following revenue sources:

NOTE: Our financial plan projects $75,000 in general administrative expense in 2000, which represents 10% of our fund-raising goal.

Medicine for Autism Today (MAT)

This non-profit organization is open to assisting the NIDS Board with fulfilling its mission through the approval of formal grant requests offered by NIDS. MAT was conceived and developed by parents of children with autism.

MAT is currently sponsoring NIDS Board symposiums around the country to begin to educate

professionals and families regarding the mission of the NIDS Board.

Charitable Organizations

Organizations such as the United Way and non-profit foundations will be targeted to assist the NIDS Board with its mission.

Health Care Organizations

Organizations such as integrated delivery systems, medical centers, hospitals, and rehabilitation centers often support initiatives such as this one.

Academic Institutions

Universities, colleges, and academic centers typically assist through financial means or through research assistance.

Insurance Companies

Insurance companies such as Blue Cross/Blue Shield and United HealthCare have offered assistance to similar initiatives through their corporate resources or their respective foundations.

IX. Financial Considerations (continued)

Private Corporations

Private enterprises such as IBM will be asked to donate either money or infrastructure (e.g., a video conferencing network to facilitate Board activities)

Private Foundations

Foundations such as the IW Folk Foundation dedicated to pediatric research will be targeted.

NIDS Parent Network (informal)

In addition to any formal assistance provided by MAT, the NIDS Board will also seek to focus the efforts of the families of NIDS children, as this is likely the largest and most motivated network at the Board's disposal at the current time.

Credit line

The Board is actively seeking a large credit line to support financial operations. The potential partners include Leviticus Alternative Fund, a philanthropic organization in New York that offers credit lines to new non-profit organizations that benefit the poor and disenfranchised.

X. Legal/Regulatory Considerations

As the NIDS Board begins to develop its business strategy and fulfill its mission, it must be aware of the following legal/regulatory considerations:

FDA Regulations

Given that the FDA is reviewing the process by which medications are approved for use in pediatrics, this aggressive timetable of this initiative could be impacted by new regulations related to the pediatric approval process.

Organizational Errors and Omissions

The NIDS Board recently approved the acquisition of a Directors and Officers liability coverage policy to minimize the financial risk associated with its management (non-clinical) actions.

Professional Liability

Given that the Board will be engaging in patient research and testing, it will also be pursuing professional liability coverage. National case law supporting vicarious liability continues to grow, thereby increasing the Board's risk of being held responsible for a clinical act or omission much the same way an HMO can be held accountable.

Other legal/regulatory risks will be identified during the development process. The Board is currently seeking to formally appoint legal counsel.

Neuro - Immune Dysfunction Syndromes

N.I.D.S

NEURO-IMMUNE DYSFUNCTION SYNDROMES
MEDICAL ADVISORY BOARD AND
RESEARCH INSTITUTE

Excerpts from the NIDS Business Plan
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Neuro - Immune Dysfunction Syndromes

N.I.D.S