IR BIOSCIENCES HOLDINGS INC
Form 10KSB/A
October 12, 2007

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-KSB/A
Amendment No. 2

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x	**Annual Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934** **For the fiscal year ended December 31, 2005**
	OR
o	**Transition Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**

COMMISSION FILE NUMBER: 33-05384

IR BIOSCIENCES HOLDINGS, INC.
(Name of Small Business Issuer in its Charter)

DELAWARE (State or Other Jurisdiction of Incorporation or Organization)	**13-3301899** (I.R.S. Employer Identification No.)
4021 N. 75th Street, Suite 201, Scottsdale, AZ (Address of Principal Executive Offices)	**85251** (Zip Code)

(480) 922-3926

(Issuer's Telephone Number, including Area Code)

Securities registered under Section 12(b) of the Exchange Act:

NONE

SECURITIES REGISTERED PURSUANT TO SECTION 12(G) OF THE EXCHANGE ACT:

COMMON STOCK, $ 0.001 PAR VALUE PER SHARE
(Title of class)

Check whether the issuer is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. o.

Check whether the issuer: (1) filed all reports required to be filed by Section 13 or 15(d) of the Exchange Act of 1934 during the past 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.

YES x NO o

Check if there is no disclosure of delinquent filers in response to Item 405 of Regulation S-B is not contained in this form, and no disclosure will be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-KSB/A or any amendment to this Form 10-KSB/A. o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes o No x

State issuer's revenues for its most recent fiscal year: $ 0

The aggregate market value of the Registrant's issued and outstanding shares of common stock held by non-affiliates of the Registrant as of March 24, 2006 (based on the average of the bid and asked prices as reported by the NASD OTC Bulletin Board as of that date) was approximately $21,208,577.

The number of shares outstanding of Registrant's Common Stock, par value $0.001 as of March 24, 2006: 69,536,319.

Documents Incorporated by reference: The information required by Part III of Form 10-KSB incorporated by reference from the Registrant's definitive proxy statement on Schedule 14A that will be filed no later than the end of the 120-day period following the Registrant's fiscal year end, or, if the Registrant's definitive proxy statement is not filed within that time, the information will be filed as part of an amendment to this Annual Report on Form 10-KSB/A, not later than the end of the 120-day period.

Transitional Small Business Disclosure Format Yes o No x

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Explanatory Note

In response to certain comments raised by the staff of the Securities and Exchange Commission, the Registrant is filing this Amendment No. 2 on Form 10-KSB/A (this "Amendment") to its Annual Report on Form 10-KSB for the year ended December 31, 2005 originally filed with the Securities and Exchange Commission (the "Commission") on March 28, 2006, and as amended by Amendment No. 1 to the Annual Report on Form 10-KSB/A filed with the Commission on March 30, 2006 (the "Original Form 10-KSB"). This Amendment contains revisions to:

- Add additional detail for clarification of descriptions of the Registrant's potential products and development thereof to Business and Management's Discussion And Analysis Of Financial Conditions And Results Of Operations;

- Update Risk Factors; and,

- Update closing sales price, number of shares outstanding and beneficial ownership.

For the convenience of the reader, this Amendment sets forth the text of the Original Form 10-KSB in its entirety. As a result of this Amendment, the certifications pursuant to Section 302 and Section 906 of the Sarbanes-Oxley Act of 2002, filed as exhibits to our 10-KSB have been revised, re-executed and re-filed as of the date of this Amendment. All information in this amendment is as of the date of the Original Filing and does not reflect any subsequent information or events occurring after the date of the Original Filing, except to reflect the corrections noted above. Accordingly, this amendment should be read in conjunction with the Company's filings made with the SEC subsequent to the filing of the Original Filing.

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FORWARD-LOOKING STATEMENTS

THIS ANNUAL REPORT ON FORM 10-KSB CONTAINS FORWARD-LOOKING STATEMENTS THAT INVOLVE RISKS AND UNCERTAINTIES. IN PARTICULAR, STATEMENTS ABOUT OUR EXPECTATIONS, BELIEFS, PLANS, OBJECTIVES, ASSUMPTIONS OR FUTURE EVENTS OR PERFORMANCE ARE CONTAINED OR INCORPORATED BY REFERENCE IN THIS REPORT. WE HAVE BASED THESE FORWARD-LOOKING STATEMENTS ON OUR CURRENT EXPECTATIONS ABOUT FUTURE EVENTS. WHILE WE BELIEVE THESE EXPECTATIONS ARE REASONABLE, SUCH FORWARD-LOOKING STATEMENTS ARE INHERENTLY SUBJECT TO RISKS AND UNCERTAINTIES, MANY OF WHICH ARE BEYOND OUR CONTROL. THE ACTUAL FUTURE RESULTS FOR IR BIOSCIENCES HOLDINGS, INC. MAY DIFFER MATERIALLY FROM THOSE DISCUSSED HERE FOR VARIOUS REASONS, INCLUDING THOSE DISCUSSED IN THIS REPORT UNDER THE HEADING "RISK FACTORS," PART II, ITEM 6 ENTITLED "MANAGEMENT'S DISCUSSION AND ANALYSIS OR PLAN OF OPERATION" AND ELSEWHERE THROUGHOUT THIS ANNUAL REPORT. GIVEN THESE RISKS AND UNCERTAINTIES, YOU ARE CAUTIONED NOT TO PLACE UNDUE RELIANCE ON SUCH FORWARD-LOOKING STATEMENTS. THE FORWARD-LOOKING STATEMENTS INCLUDED IN THIS REPORT ARE MADE ONLY AS OF THE DATE HEREOF. WE DO NOT UNDERTAKE AND SPECIFICALLY DECLINE ANY OBLIGATION TO UPDATE ANY SUCH STATEMENTS OR TO PUBLICLY ANNOUNCE THE RESULTS OF ANY REVISIONS TO ANY OF SUCH STATEMENTS TO REFLECT FUTURE EVENTS OR DEVELOPMENTS. WHEN USED IN THE REPORT, UNLESS OTHERWISE INDICATED, "WE," "OUR," "US," THE "COMPANY" OR "IMMUNEREGEN" REFERS TO IR BIOSCIENCES HOLDINGS, INC. AND ITS SUBSIDIARY, IMMUNEREGEN BIOSCIENCES, INC.

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PART I

Item 1. Description of Business

Overview

IR BioSciences Holdings, Inc. is a development stage biotechnology company. Through our wholly-owned subsidiary ImmuneRegen BioSciences, Inc., we are engaged in the research and development of potential drug candidates, Homspera™ and its derivatives, Radilex™ and Viprovex™. Our goal is to develop these potential drug candidates to be used as possible countermeasures for homeland security threats, including radiological, chemical and biological agents, such as influenza and anthrax. We hope there may exist not only a market for products related to biodefense through governmental purchasing, but there also may exist a potential commercial market for treatments of cancer treatment side-effects and seasonal influenza.

Our patents, patent applications and continued research are derived from discoveries made during research studies related to the function of Substance P performed before the formation of the Company. These studies were funded by the Air Force Office of Scientific Research (AFOSR) in the early 1990s and were conducted by research scientists, including our co-founders Drs. Mark Witten and David Harris. In the course of research on Substance P, these scientists created a number of synthetic analogues, structural derivatives with slight chemical differences, for study. One of these, which we have named Homspera, is the basis for our drug development efforts and our intellectual property. All of our research and development efforts are early, pre-clinical stage and Homspera has only undergone exploratory studies to evaluate its biological activity in small animals. There can be no assurance that our interpretation of the results of our studies will prove to be accurate after further testing and our beliefs regarding the potential uses of our drug candidates may never materialize.

Our current focus is on the development of two potential formulations derived from Homspera, Radilex and Viprovex.

We are researching Radilex for use as a potential treatment for acute exposure to radiation. To date we have sponsored seven studies and co-sponsored three studies all of which were conducted utilizing rodents. The results of these studies suggest Radilex may play a role in increased survival among tested rodents following exposure to lethal doses of gamma radiation. We believe that Radilex, if developed, may be an acceptable candidate to be marketed to governmental agencies for procurement. Further, we believe that a commercial market may exist for the use of Radilex as it relates to the treatment of radiation-induced side effects of cancer treatments, either as a stand alone treatment or as a co-therapeutic agent to be used with other therapies.

Viprovex is being researched by us for use in potential treatments of exposure to biological agents, such as infectious disease, which include influenza and anthrax. Based on early studies on Homspera and existing literature on Substance P, we are researching the efficacy of Viprovex as a potential treatment for exposure to chemical agents, such as formalin. To date we have sponsored three studies related to the treatment of influenza, three on the exposure to anthrax spores and one on exposure to formalin. We believe the results of these studies indicated potential efficacy in the use of Viprovex as both a stand alone treatment and an adjuvant, to be used in conjunction with other drugs. If Viprovex can be developed, we believe that potential applications may exist for sale to governments for the treatment of exposure to anthrax and pandemic influenza. In addition, we believe that potential commercial opportunities may exist for the treatment of seasonal influenza and other viral or bacterial infections, either as a stand-along drug or as an adjuvant to other existing drugs.

To date we have submitted preliminary study data to the U.S. Food and Drug Administration (FDA) and have been issued two Pre-Investigational New Drug (PIND) numbers, one for the potential use of Radilex in the treatment of

acute radiation syndrome and the other for the potential use of Viprovex in the treatment of avian influenza.

We have filed patent applications and provisional patent applications, for the use of Homspera and derivatives thereof. We own two issued U.S. and two issued foreign patents and two pending Patent Cooperation Treaty (PCT) applications, seven pending U.S. provisional patent applications and 16 pending foreign provisional patent applications.

Our potential drug candidates, Radilex and Viprovex, are at early, pre-clinical stages of development and may not be shown to be safe or effective and may never receive regulatory approval. Neither Radilex nor Viprovex have yet been tested in large animals or humans. There is no guarantee that regulatory authorities will ever permit human testing of Radilex, Viprovex or any other potential products derived from Homspera. Even if such testing is permitted, none of Radilex, Viprovex or any other potential drug candidates, if any, derived from Homspera may be successfully developed or shown to be safe or effective.

The results of our pre-clinical studies and clinical trials may not be indicative of future clinical trial results. A commitment of substantial resources to conduct time-consuming research, pre-clinical studies and clinical trials will be required if we are to develop any commercial applications using Homspera or any derivatives thereof. Delays in planned patient enrollment in our future clinical trials may result in increased costs, program delays or both. None of our potential technologies may prove to be safe or effective in clinical trials. Approval of the FDA, or other regulatory approvals, including export license permissions, may not be obtained and even if successfully developed and approved, our potential applications may not achieve market acceptance. Any potential applications resulting from our programs may not be successfully developed or commercially available for a number of years, if at all.

To date, we have not obtained regulatory approval for or commercialized any applications using Homspera or any of its derivatives. We have incurred significant losses since our inception and we expect to incur annual losses for at least the next three years as we continue with our drug research and development efforts.

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Substance P And Homspera™

Our patents, patent applications and continued research are derived from discoveries made during research studies related to the function of Substance P, which is found in the body and has a large number of actions. These studies, performed prior to our formation, were funded by the Air Force Office of Scientific Research (AFOSR) in the early 1990s and were conducted by research scientists, including our co-founders Drs. Mark Witten and David Harris. In the course of this research, these scientists created for study a number of analogues, or structural derivatives with slight chemical differences, of Substance P. One of these analogues of Substance P, which we have termed Homspera, is the basis for our research and development of potential drug candidates.

Substance P

The elements carbon, oxygen, nitrogen and hydrogen can be combined to form amino acids, a basic building block of life. When amino acids are combined through a biochemical process they form what are called peptides or proteins. Proteins play a number of fundamental roles in living organisms, from structural to messaging between cells. When components of the nervous system use chemicals to transmit signals between nerves and brain cells to propagate signaling throughout the body, those chemicals are called neurotransmitters. When peptides are released by nerves cells or other cells and modulate this neurotransmission, they are termed neuropeptides.

One such neuropeptide is Substance P. Substance P is a relatively small peptide made of just eleven amino acids. Substance P was discovered in 1931 and found to have local blood-pressure reducing effects. The peptide is difficult to isolate, and consequently was ignored for tens of years. When science developed to the point that peptides could be recognized by their amino acid structures, Substance P was one of the first identified. The amino acid sequence (using the standard three-letter acronyms for amino acids) of Substance P is presented below:

Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu-Met-NH_2.

Neuropeptides, such as Substance P, were originally identified as being distributed throughout the peripheral and central nervous systems of experimental animals, and then of humans. To date, Substance P has also been shown to be produced in non-neuronal cells such as human endothelial cells, Leydig cells, enterochromaffin cells, epithelial cells, fibroblasts, keratinocytes, intestinal and airway smooth muscle cells, inflammatory and immune cells, and in cells of the female reproductive system.

In early research Substance P was revealed as playing a key role in the transmission of pain. Later on, Substance P was identified as being involved in the pathophysiology of psychiatric disorders, like anxiety and depression. Additionally, Substance P has been shown to be involved in a number of physiological processes, such as blood vessel and smooth muscle contractions, and in the levels and responses of the cells of the blood and immune system.

Substance P produces this wide variety of effects by acting through three different molecular receptors, located on the surface membrane of sensitive cells. These receptors are called NK1, NK2 and NK3 receptors, and binding of Substance P to one receptor subtype or another will cause different chemical signaling to occur both inside and outside cells. These receptor binding differences are believed to be responsible for the different physiological results following the stimulation of the different receptor subtypes.

Homspera

Within a few years following the discovery of the amino acid sequence of Substance P, numerous synthetic analogues were being produced in an attempt to better understand how the structure and function of the molecule were related. One particular analogue was produced by the replacement of the amino acid glycine (Gly) with Sarcosine (Sar or

N-methyl glycine) at the ninth position and the introduction of oxidized methionine (Met(O_2)) in place of methionine (Met) at the eleventh position. The resulting peptide, still 11 amino acids long, but now with a slightly different molecular weight, is thus called Sar^9, Met $(O_2)^{11}$-Substance P. The amino acid sequence for Homspera is presented below:

Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Sar-Leu-Met(O_2)-NH_2.

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It is these specific chemical alterations that are presumably responsible for the different physiological actions of Homspera versus endogenous Substance P. In fact, Sar^9, Met $(O_2)^{11}$-Substance P was first synthesized in an attempt to make chemicals that had specific distinctions in their activity from that of the parent Substance P molecule.

Homspera, or Sar^9, Met $(O_2)^{11}$-Substance P differs from Substance P in at least two ways. It is reported to be active at only the NK1 receptor, and to be more resistant to the enzyme that usually breaks down Substance P and thereby terminates its action. Thus Sar^9, Met $(O_2)^{11}$-Substance P is both more specific than Substance P, and also more persistent in the body.

In December 2004 we filed an application with the US Patent and Trademark Office in an effort to trademark the name Homspera to refer to Sar^9, Met $(O_2)^{11}$-Substance P for its potential usage in a number of applications. Our application is still pending.

Radilex™ and Viprovex™

In the early AFOSR studies, it was observed that the exposure of animals to JP-8 jet fuel resulted in pathological changes in the lungs and immune systems of those exposed. Homspera was administered to the test animals after prolonged exposure to the jet fuel. Based on the results of these studies, we believe that the administration of Homspera prevented some of the harmful effects of the jet fuel exposure in the lungs, as well as having a positive effect on the immune system. However, there is no guarantee that our interpretation of the results of these studies will prove to be accurate after further testing.

Based on our interpretation of these results, our current focus is on the development of two potential drug applications, Radilex and Viprovex. We have created the trade names Radilex and Viprovex to more easily differentiate the potential applications with respect to their development and potential future market opportunities. Although the active ingredient, Homspera, is chemically equivalent in both Radilex and Viprovex, their administration and their formulations differ.

We are researching Radilex for use as a potential treatment for acute exposure to radiation. To date we have sponsored seven studies and co-sponsored three studies all of which were conducted utilizing rodents. We believe the results of these and other studies suggest Radilex may play a role in increasing an individual's ability to overcome the effects of radiation, and, in the cases of exposure to potentially lethal radiation, to play a role in increased rates of survivability. Based on the sum of these studies, we believe that Radilex, once and if developed, could be an acceptable candidate to be purchased by governmental agencies for national distribution in the event of a significant nuclear or radiological threat. Further, we believe that a commercial market may exist for the use of Radilex as it relates to the treatment of radiation-induced side effects of cancer treatments, either as a stand alone treatment or as a co-therapeutic agent to be used with other treatments.

Viprovex is being researched by us for use in potential treatments of exposure to biological agents, such as anthrax and infectious diseases, including influenza. Based on early studies on Homspera and existing literature on Substance P, we are also researching Viprovex as a potential treatment for exposure to chemical agents, such as formalin. Formalin, a highly toxic chemical, is a solution of formaldehyde gas dissolved in water and used industrially. To date we have sponsored three studies related to the treatment of influenza, three on the exposure to anthrax spores and one on exposure to formalin. We believe the results of these studies indicated potential efficacy in the use of Viprovex as both a stand alone treatment and to be used in conjunction with other drugs. If Viprovex can be developed, we believe that potential applications may exist for sale to governments for the treatment of exposure to anthrax and pandemic influenza. In addition, we believe that potential commercial opportunities may exist for the treatment of seasonal influenza and other viral or bacterial infections, either as a stand-alone drug or in conjunction with other existing

drugs.

Applications

Our initial pre-clinical applications that we are researching are in the treatment of the effects on the body caused by (i) exposure to radiation (Radilex) (ii) infectious disease and harmful biological materials (Viprovex) and (iii) harmful chemical agents (Viprovex). In addition to these three potential applications, we continue to explore the potential capabilities of Homspera and strive to better understand the mechanisms of this compound in order to further our development efforts with regard to not only our current application research, but also potential future applications.

To date we have sponsored seven radiation studies and co-sponsored three radiation studies all of which were conducted utilizing rodents. We have sponsored three studies on the potential treatment of anthrax exposure and one study on avian influenza all of which were conducted utilizing rodents. We have also sponsored one chemical study in an attempt to determine initial indications of efficacy on the treatment of formalin exposure.

All our product candidates are in the pre-clinical stage of development. They have only been introduced to FDA via the pre-IND filings, submissions to which the FDA offers no judgment thereon. To date we have been issued two Pre-Investigational New Drug (PIND) numbers by the U.S. Food & Drug Administration (FDA) - one for the potential use of Radilex in the treatment of acute radiation syndrome and one for the potential use of Viprovex in the treatment of avian influenza. The table below illustrates our current product candidates and their current stage of development within the FDA approval process.

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Product Candidate	Pharmacological Identification	Animal Safety	Pre-Clinical Mechanistic	Phase I	Phase II	Phase III
Acute Radiation Syndrome						
Radilex	In-progress	Planned	In-progress	—	—	—
Infectious disease						
Viprovex	In-progress	Planned	In-progress	—	—	—
Chemical exposure						
Viprovex	In-progress	Planned	Planned	—	—	—

The preliminary results of our pre-clinical studies using Radilex or Viprovex may not be indicative of results that will be obtained from subsequent studies or from more extensive trials. Further, our pre-clinical or clinical trials may not be successful, and we may not be able to obtain the required regulatory approvals in a timely fashion, or at all. See "Risk Factors."

Radilex

All of our product candidates based on Radilex are in the pre-clinical stage of development. On January 14, 2004, we received a Pre-Investigational New Drug Application (PIND) number for the use of Radilex (PIND No. 63,255) in the treatment of acute radiation syndrome.

To date we have sponsored seven radiation studies and co-sponsored three radiation studies all of which were conducted utilizing rodents to study dose response to radiation, the impact on survival and to distinguish survival response using different forms of drug delivery. In each of these studies mice were exposed to varying levels of radiation and the Radilex was aerosolized in water and administered to the test subject animals by inhalation.

Radiation is emitted electromagnetic energy. Excessive exposure to ionizing radiation over a short period of time, as is the case in nuclear or radiological attacks, leads to the development of radiation sickness, or Acute Radiation Syndrome (ARS). Exposure to lower doses of radiation may, either by design or as a side effect of cancer treatment, result in the destruction of bone marrow cells responsible for maintaining the levels of red blood cells, white blood cells and platelets, which are vital for the formation of blood clots, in the circulation, resulting in compromised oxygen carrying capacity, diminished immune system function, and uncontrollable bleeding.

These bone marrow cells are called hematopoietic stem cells, and they can multiply and mature into precursor cells to the B-cells and T-cells of the immune system, or into precursors of the red blood cells and of the granulocytes and macrophages, which are also of the immune system, and megakaryocytes, which produces platelets. Thus all circulating cells of the immune system, red blood cells and platelets derive from these stem cells.

In studies to date we have collected data that we believe suggests that Radilex shows efficacy in treating ARS by combating neutropenia and thrombocytopenia, which is the decrease in blood levels of white blood cells and platelets, the major medical conditions associated with acute exposure to radiation. Loss of these cells results in increased sensitivity to infection and to uncontrolled bleeding, both of which can be potentially life-threatening. Further, as treatment for cancer often includes radiation treatment, we believe that the potential also exists for Radilex to be used for cancer patients as a stand alone treatment or a co-therapeutic agent to be used with other drugs as treatment.

Data collected in studies performed at the Oak Ridge National Laboratory in 2006, we believe, revealed that Radilex not only prolonged survival of animals exposed to lethal gamma irradiation, but also appeared to have increased platelet concentrations in surviving animals.

There is also preliminary research data showing that the activity of a specific enzyme (poly-(ADP-ribosyl) polymerase, or PARP), may be responsible for repairing DNA that has been damaged by radiation can be modified by Substance P. When damage is severe, the activation of this enzyme becomes too much for the cell to support, and the cell triggers its own destruction. The chain of events that result in this destruction is called apoptosis, a process of deliberate life termination that a cell undergoes following exposure to high levels of stress, and agents that can control the rate of apoptosis are of significant importance in controlling the functioning of organs and organisms. If a cell can be kept alive long enough to repair cellular damage, it might be of more value to the organism.

Based on the above referenced, and other, data, we believe that one possible mechanism by which Radilex is able to prolong survival in animal models (either in addition to its effect on stem cells or perhaps as a mechanism by which it impacts stem cells), is by modulating the activities of the PARP-1 enzyme within cells. By possibly preventing cells from dying, Radilex may be effective in treating the impact of cell radiation, thereby decreasing the likelihood of death.

Further, we believe that our survival data from irradiated mice studies and mechanistic studies in cell culture have shown indications of hematopoietic stem cell replenishment of circulating leukocytes and platelets, which could be of value in radiation-treated cancer patients.

Acute total body irradiation exposure studies have been performed at the University of Arizona Cancer Center and at Oak Ridge National Laboratories (ORNL). These studies show that radiation destroys the immune system resulting in pneumonia and death, and that Radilex, we believe demonstrates efficacy at reversing the loss of white blood cells that comprise the immune system, as well as platelets necessary to control blood clotting, subsequently leading to an increase in survival rates.

We believe these animal studies provide support for our continued effort to research and develop Radilex to treat the effects of exposure to radiation. However, there is no assurance that our interpretation of the results of the studies will prove to be accurate after further testing.

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Viprovex

All of our product candidates based on Viprovex are in the pre-clinical stage of development. We are researching the efficacy of Viprovex as a potential treatment, either as a stand alone application or as co-therapeutic treatment, for exposure to various biological agents, such as infectious disease, including influenza and anthrax. We are also researching the efficacy of Viprovex as a potential treatment for exposure to chemical agents, such as formalin. Formalin, a highly toxic chemical, is a solution of formaldehyde gas dissolved in water and used industrially.

Unlike Radilex, we are currently formulating Viprovex in a buffered saline solution as its preferred method of administration is intranasal.

Biological Exposure Applications

Infectious Disease - Seasonal and Pandemic Influenza

We believe of management that results from our studies may reveal the potential ability of Viprovex to enhance flu therapies, minimize the respiratory impact of influenza infection and augment the capability of vaccination to induce a protective immune response.

In October 2003 the AFOSR sponsored preliminary studies with the Hong Kong influenza virus (A/Hong Kong/8/68) and Viprovex at the University of Arizona, Arizona Health Sciences Center, Lung Injury Laboratory. We believe that these studies suggest that when mice were exposed to the irritant JP-8 jet fuel and then inoculated with the Hong Kong respiratory virus (HKV), they experience elevated levels of inflammatory cells in their lungs. These levels were reduced in animals also treated with Viprovex. In contrast to control animals exposed to the virus the JP-8 treated animals also treated with Viprovex, did not develop the clinical symptoms of viral infection, which included increases in alveolar macrophages and neutrophils in broncho-alveolar lavage fluid. These cells are components of the immune system that are expressed out of the blood and into the fluid inside the lungs coating the alveoli. The alveoli, found in the respiratory zone of the lungs, are primary sites of gas exchange where blood and air exchange oxygen and carbon dioxide carried by red blood cells. The fluid is acquired and assayed by washing lavage the lungs with liquid and assessing the cells and chemicals in this wash fluid. Animals treated with Viprovex also exhibited lower levels of leukotriene B4 (LTB4), a chemical released by white blood cells during an immune response, than animals not treated with Viprovex. Elevated LTB4 would attract the inflammatory cells, particularly neutrophils, which would follow infection with virus. Electron micrographs showed healthier, normal appearing cells in the airways with no virus particles in the Viprovex-treated animals, in contrast to the HKV/JP-8 controls, suggesting, in our opinion, that Viprovex actually prevented viral replication and pathology, perhaps by stimulating the pulmonary alveolar macrophages to actively attack, engulf and destroy the virus more effectively. Without virus particles in the lungs, there would be no need to mount an immune response. Based on the results of this study, we believe that Viprovex may be potentially used to increase the ability of the body's own immune system to naturally fight off flu strains. Thereby, opening up the possibility that Viprovex could be used either as a stand alone treatment or as an adjunct to a vaccine or other therapy.

On November 29, 2005 we applied for a PIND from the Department of Health and Human Services (HHS) for the use of Viprovex in the treatment of avian influenza. The PIND number for the use of Viprovex in treating avian influenza was issued on December 19, 2005 (PIND No. 73,709).

Subsequently, we have sponsored three influenza studies conducted at Virion Systems, Inc, one of which is still ongoing, utilizing rodents to test the efficacy of Viprovex in treating the avian influenza A/Wuhan/359/95 (H3N2), a model system for studying the H5N1 avian influenza.

In our opinion, the data acquired to date in examining the effect of Viprovex on influenza infection suggests an anti-viral action occurs in lungs and, more noticeably, in nose. Further, in conjunction with the suggested anti-viral effect, animal weights and temperatures were normalized. Differences in cytokines (small peptide signaling molecules released by cells of the immune system to mediate inflammation and immune responses) such as certain interleukins and interferons were also witnessed. In the opinion of management, such Viprovex-induced changes in immune response as evinced by cytokine signals demonstrate the potential efficacy of Viprovex. Based on our results, we believe that Viprovex may show efficacy as a stand alone drug in the treatment of influenza. Further, when used in conjunction with a neuraminidase inhibitor, currently the most effective pharmacological agents (zanamivir (Relenza®, GlaxoSmithKline) and oseltamivir (Tamiflu®, Roche) are neuraminidase inhibitors) to treat influenza (by inhibiting an enzyme necessary for infectivity), Viprovex might be an effective adjuvant therapeutic on treating or preventing influenza.

There is no assurance that our interpretation of the results of the studies will prove to be accurate after further testing.