



First U.S. Biomedical Seminar on the Transportation of Infectious and Diagnostic Substances

Co-Editor's Note

The following summaries of the presentations from this meeting on the shipment of infectious and diagnostic substances were provided by World Courier, the company that hosted the seminar. As an attendee at this meeting, I believe that the summaries are accurate and will be interesting and useful to Association members.

Ira F. Salkin

Abstract

The globalization of the biopharmaceutical industry over the past 15 years has provided unprecedented opportunity for laboratories and research organizations to tap into new geographies and extend the scope of clinical trials and studies. At the same time, pressing biosafety issues that potentially put at risk both those handling the specimens and the public at large, has led to a profusion of directives—and sometimes conflicting information—from within the industry, governmental bodies, regulatory agencies, and transporters themselves.

Introduction

The first U.S. Biomedical Seminar on the Transportation of Infectious and Diagnostic Substances, hosted by World Courier, addressed many of the critical issues associated with this increasingly complex and critical aspect of clinical trial management.

Held in Miami Beach, Florida on April 20, 2001, the seminar brought together more than 200 industry

practitioners from as far away as Japan with principals from the air transportation industry and various regulatory bodies.

Chairman and moderator for the event was Dr. Jonathan Y. Richmond, Director of the Office of Health and Safety at the Centers for Disease Control and Prevention in Atlanta and an internationally recognized consultant and educator in the field of biosafety and training. Dr. Richmond was joined on the podium by speakers representing the Centers for Disease Control, IATA, the FAA, U.S. Customs, the FDA, the Pan-American Health Organization, Lab-Corp and Bristol-Myers Squibb Pharmaceutical Research Institute (see Table 1), with each sharing his or her unique perspective and personal insight on the issues.

"The transportation of diagnostic samples is an extremely complex issue that relies on the knowledge and expertise of many different organizations and individuals in the course of even a single shipment," says Wayne B. Heyland, president of World Courier Group. "Our objective in presenting these seminars is to educate and to examine all sides of the issue."

By the conclusion of the conference, participants had a better understanding of: current transportation regulations and the reasons for their implementation; the need for an ongoing reassessment of this evolving area of legislation; each organization's unique role in the transportation process; their organization's need to comply with federal and international regulations as well as the liabilities and penalties for noncompliance; and the integral role that transportation can play in the success of a study.

Table 1

Seminar Agenda & Speakers' Topics
U.S. Biomedical Seminar on the Transportation of Infectious and Diagnostic Substances
Wyndham Miami Beach Resort, Miami, Florida, Friday, April 20, 2001

Morning Session	Afternoon Session
<p>Mr. Mark Hemphill, Acting Chief, External Activities, Centers for Disease Control and Prevention...on regulatory activities of the CDC including Import Permits, Laboratory Registration, and the Select Agent Transfer Program</p>	<p>Dr. José R. Cruz, Regional Advisor, Laboratory & Blood Services, Pan-American Health Organization...on the global perspectives and realities of transporting infectious and diagnostic substances, particularly with respect to the emerging nations of Latin America</p>
<p>Mr. William Wilkening, Manager, Dangerous Goods & Cargo Security Division, Federal Aviation Administration...on the compliance enforcement trends of the FAA including inspections, incidents, and outreach programs</p>	<p>Mr. Richard Rubio, Senior Customs Inspector, United States Customs Service, Office of Field Operations...on the Code of Federal Regulations (CFR) governing the transport of infectious substances, preclearance inspection, enforcement and penalties</p>
<p>Mr. Jean Abouchaar, Assistant Director, Cargo Regulatory Industry Affairs, International Air Transport Association...on the mandate and role of IATA, and new provisions affecting the transportation of diagnostic specimens scheduled for July 2001</p>	<p>Ms. Christine Humphrey, Compliance Officer, U.S. Food and Drug Administration...on import and export procedures, laws, and regulations affecting the transportation of regulated products, including the implication of notices of sampling, failure to hold/redeliver, and the FDA's Import Alert Authority</p>
<p>Mr. Remy A. Rodas, Esq., Attorney, Ivey Barnum & O'Mara, LLC...on the liability exposure faced by shippers of diagnostic specimens and key preventive measures</p>	<p>Mr. Jeff O'Connor, Managing Director, American Airlines—Safety, Security and Environmental Compliance...on reducing the potential of an airline's refusal of a shipment and successfully transporting diagnostic specimens</p>
<p>Capt. Ed Sprenkle, Member and representative for International Federation of Airline Pilots, Dangerous Goods Committee...on the position of commercial pilots and airlines in handling and refusing diagnostic specimens; undeclared shipments and the "worst case" scenario for flight crews and passengers; and the potential impact of airborne pathogen leakage in new generation aircraft</p>	<p>Mr. Steven J. Olsen, Senior Manager, Clinical Pharmacology/Experimental Medicine, Bristol-Myers Squibb Pharmaceutical Research Institute...on the need for stronger relationships between sponsors, CROs, investigator sites, labs, and service suppliers in meeting the demands of today's competitive environment, and in recruiting subjects and managing studies in developing nations</p>
	<p>Ms. Denise McFadden, Director, Business Development, Infectious Disease Clinical Trials, LabCorp...on the challenges of conducting successful clinical trials in Central and Latin America, including the trends, the timing, and the logistics</p>

Summaries of Presentations

Mark Hemphill, Acting Chief, External Activities, Centers for Disease Control and Prevention (CDC)

In this presentation, Mr. Hemphill outlined the fundamental criteria of the two key CDC initiatives most likely to impact biomedical practitioners—the need to obtain Import Permits and to properly package and label any infectious substances imported into or

transferred within the United States and the Select Agent Transfer Program. The latter program has been designed to identify, regulate, and track biological agents that may pose a threat to public safety and establishes guidelines and procedures for the registration, transferring, tracking, handling, and disposal of these agents. Underscoring the seriousness with which this program is regarded, Mr. Hemphill cautioned that non-compliance can result in organizational fines of up to \$500,000 per event.

Mr. William Wilkening, Manager, Dangerous Goods & Cargo Security, Division, Federal Aviation Administration (FAA)

In this presentation, Mr. Wilkening drew on FAA statistics to reinforce industry's need to practice proper packaging procedures when preparing hazardous substances for shipment. Of almost 1,000 "incidents" involving dangerous goods shipments reported in 1999, the predominant reason for packaging failures was faulty closure/seal leakage.

With an estimated 75,000 dangerous goods shippers in the United States, the FAA supports the efforts of the federal government and the CDC in monitoring and maintaining a safe environment for the shipping of hazardous materials. The FAA's Dangerous Goods and Cargo Security (DG/CS) Program, an initiative currently administered by Mr. Wilkening, combines enforcement, trend analysis, and outreach programs to ensure that shipments comply with existing regulations. Under this program, the FAA investigated almost 3,000 cases last year, resulting in the collection of almost \$8 million in fines.

Mr. Jean Abouchaar, Assistant Director, Cargo Regulatory Industry Affairs, International Air Transport Association (IATA)

With over 270 member airlines worldwide carrying 98% of all air cargo, IATA sets the standards for the shipping of dangerous goods. Its mandate is to work with governments and other international organizations to develop practical, yet economically sound, regulations that advance air safety.

In this presentation, Mr. Abouchaar previewed pending changes to IATA's Dangerous Goods Regula-

tions that impact the biomedical community—changes scheduled to come into effect on July 1, 2001 including the reassignment of diagnostic specimens to category UN 3373 and infectious or potentially infectious specimens to UN 2814 or UN 2900. Other changes include redefinition of infectious substances to encompass all body fluids without risk group 4 pathogens, an increase to 1 litre in the maximum quantity that may be carried (special provision A81), and new provisions related to certain sterilization devices (special provision 131).

Reinforcing the need for proper packaging and labelling, Mr. Abouchaar reviewed important changes to package marking and testing for infectious substances that came into effect January 1, 2001 (4G designation). He also fielded a variety of questions on the adoption of Packing Instruction 650 (minimum packaging for potentially biohazardous materials) by the International Civil Aviation Organization (ICAO), and the differences between it and Packing Instruction 6.2 for infectious substances.

Mr. Remy A. Rodas, Esq., Attorney, Ivey Barnum & O'Mara, LLC

Using a hypothetical case study, Mr. Rodas convincingly demonstrated the legal need for diligence, adequate training, and established procedures in the workplace to minimize the biomed's exposure to liability.

In his fictitious account of injuries suffered by an airline worker who is unwittingly contaminated by incorrectly packaged and labelled infectious specimens, Mr. Rodas vividly described the "four knocks on the door" that his shipper, a San Francisco hospital, would receive: the first from the FAA, the next from the media, the third from the airline's attorneys, and the last from the victim's personal injury lawyer—as well as the potentially weighty financial penalties and public relations nightmares to which the hospital would be subject.

He concluded with an overview of key preventive measures shippers should implement and enforce within their work environment including staff training, the development of an in-house "checks and balances" system, the preparation of adequate emergency response procedures, and consistent compliance with shipping protocols and regulations.

He further recommended that shippers maintain detailed in-house records of all employee training.

Capt. Ed Sprenkle, Member and representative for International Federation of Airline Pilots, Dangerous Goods Committee

In the final presentation of the morning, Captain Sprenkle provided an extremely informative and unique "cockpit" perspective on the need for safety and security when transporting potentially dangerous diagnostic specimens aboard commercial aircraft. He boldly suggested that fear, combined with a lack of adequate training and awareness by airline employees, often erroneously resulted in "refusal solutions" by pilots and cargo personnel who can and do reject shipments, sometimes without adequate reason.

In light of air tragedies such as the ValuJet crash in Florida, caused by exploding—and undeclared—oxygen generators, he also called for better training for shippers, encouraging the health care industry to assume the lead in assuring compliance.

Captain Sprenkle concluded by elaborating on important technical concerns—including the ease with which airborne pathogens can be returned to the passenger cabin in new generation aircraft—that may have contributed to some airlines' refusal to carry specific types of dangerous goods. This, according to Captain Sprenkle, poses the most serious danger in the opinion of pilots—the increase in undeclared shipments as shippers knowingly attempt to circumvent airline policy.

Dr. José R. Cruz, Regional Advisor, Laboratory & Blood Services, Pan-American Health Organization

In keeping with a secondary theme of the seminar—the ongoing development of business opportunities within the Americas—Dr. Cruz painted a clear and concise picture of the realities of conducting biomedical research in Latin America and the Caribbean.

He detailed the primary constraints faced by biomedical organizations operating in these areas: national regulations and governmental awareness and involvement; lack of adequately trained lab personnel; lack of trained service personnel including couriers, airline personnel, customs officials, and customs brokers; diffi-

culties in procuring appropriate laboratory and packaging materials; the considerably higher cost of services including transportation costs; and the lack of financial resources to rectify these situations.

Dr. Cruz also reiterated some of the key concerns articulated by other members of the panel, particularly the threat of bioterrorism and danger to personnel and public safety, that potentially can arise in a less regulated environment.

Mr. Richard Rubio, Senior Customs Inspector, United States Customs Service, Office of Field Operations

In this presentation, Mr. Rubio outlined the role of U.S. Customs in enforcing the provisions of the Code of Federal Regulations (CFR) that relate specifically to the transport of infectious substances on passenger or air cargo aircraft (Title 49, Parts 107-180, Subchapter C, Class 6, Division 6.2).

Mr. Rubio then walked participants through the importation and clearance process. He reinforced the need for correct paperwork that clearly and accurately describes the nature of the substances being imported, and for the correct packaging and labelling, without which shipments can be subjected to inspections, delays, and potential seizure by Customs.

He concluded with an overview of the civil penalties and monetary liability to which companies that knowingly violate federal hazardous materials transportation law are subject.

Ms. Christine Humphrey, Compliance Officer, U.S. Food and Drug Administration (FDA)

The focus of Ms. Humphrey's presentation was meeting compliance requirements for the importation of FDA-regulated products, notably biological products including blood/blood components, drugs, medical devices, food, and electronic products. She elaborated on the specific regulatory requirements that pertain to each product grouping, the conditions under which they are subject to licensure, the articles of law to which they are subject, and the data required for importation.

She then discussed legislation affecting substances imported for future export (such as drug and biologic components), the necessary steps to be taken by the

importer, and the ramifications of noncompliance with FDA requirements.

Ms. Humphrey concluded with an overview of the various mechanisms that the FDA and U.S. Customs have put in place to regulate the importation and transport of controlled articles. These include Notices of Sampling, Failure to Hold/Redeliver, Customs Entry Bond Conditions, and Import Alert Authority. In each case, she cautioned, noncompliance can result in serious repercussions of either a monetary or operational nature.

Mr. Jeff O'Connor, Managing Director, American Airlines—Safety, Security and Environmental Compliance

Mr. O'Connor's presentation addressed the keys to avoiding shipment refusal by airlines—adherence to proper packaging protocol, and the preparation of clear, correct, and accurate paperwork.

He explained that the best way to circumvent the airlines' "10,000 ways to refuse a shipment" was, plainly and simply, to "dot all the *i*'s and cross all the *t*'s" when completing the airline's air waybill and the Shipper's Declaration for Dangerous Goods. He also reinforced the need for appropriate packaging, marking, and labelling to help mitigate the fears and concerns of airline personnel.

In closing, Mr. O'Connor reiterated many of the conclusions drawn by other members of the panel, citing a need for better and more consistent training of everyone involved in the shipping process—from laboratory personnel to transportation and airline staff to customs officials.

Mr. Steven J. Olsen, Senior Manager, Clinical Pharmacology/Experimental Medicine, Bristol-Myers Squibb Pharmaceutical Research Institute

In his opening remarks, Mr. Olsen provided participants with an interesting juxtaposition between the "old" approach of containing a clinical trial within a single country, and the "new" and highly competitive business model which calls for shorter developmental time, the maximization of resources and intellectual

capital, and a global perspective on the part of trial sponsors. He enumerated the many changes associated with this evolution, including governmental intervention and industry regulation designed to ensure uniform and acceptable practices on a worldwide level as well as the rise of more accurate laboratory testing methods and markers.

Mr. Olsen then offered a compelling argument that infectious disease trials require global coordination that can only be effected by strong communications between all parties associated with the study—the sponsor, the investigator sites, central lab, and the transportation providers—particularly in those emerging geographies where patient recruitment has been based on disease incidence.

Ms. Denise McFadden, Director, Business Development, Infectious Disease Clinical Trials, LabCorp

Speaking on the challenges of conducting successful clinical trials in Central and Latin America, Ms. McFadden opened her presentation with a discussion on the rationale behind sponsors' growing interest in these venues. The expansion of the company's global reach, the ability to fulfil the regulatory requirements of larger geographies with fewer trials, time and cost considerations, and the availability of naive subjects were key reasons cited.

Ms. McFadden then drew on her experiences in coordinating international studies in countries such as Brazil, Argentina, and Chile to describe the challenges faced by companies interested in conducting research in this region, and the many decisions that must be made in advance of the study.

She explained that issues such as country and site selection; cultural, time and temperature differences; airline schedules and transportation capabilities; import and export requirements; the selection of local versus central laboratories; study timelines; and data management issues are some of the considerations that can have a serious impact on the outcome of a study. She further cautioned that the logistics of initiating studies in Central and Latin America cannot typically be expedited as quickly as in other parts of the world.