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# Development of Self-Remediating Packaging for Safe and Secure Transport of Infectious Substances

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**Abstract**

As George W. Bush recognized in November 2001, "Infectious diseases make no distinctions among people and recognize no borders." By their very nature, infectious diseases of natural or intentional (bioterrorist) origins are capable of threatening regional health systems and economies. The best mechanism for minimizing the spread and impact of infectious disease is rapid disease detection and diagnosis. For rapid diagnosis to occur, infectious substances (IS) must be transported very quickly to appropriate laboratories, sometimes located across the world. Shipment of IS is problematic since many carriers, concerned about leaking packages, refuse to ship this material. The current packaging does not have any ability to neutralize or kill leaking IS. The technology described here was developed by Sandia National Laboratories to provide a fail-safe packaging system for shipment of IS that will increase the likelihood that critical material can be shipped to appropriate laboratories following a bioterrorism event or the outbreak of an infectious disease. This safe and secure packaging method contains a novel decontaminating material that will kill or neutralize any leaking infectious organisms; this feature will decrease the risk associated with shipping IS, making transport more efficient.

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# Acronyms and Abbreviations

| | |
|---|---|
| ATA | Air Transport Association |
| BTS | Bureau of Transportation Statistics |
| BW | biological weapons |
| CFU | Colony Forming Units |
| DGR | *Dangerous Goods Regulations* |
| DOT | Department of Transportation |
| FAA | Federal Aviation Administration |
| IATA | International Air Transport Association |
| ICAO | International Civil Aviation Organization |
| IS | infectious substances |
| PEG | polyethylene glycol |
| SNL | Sandia National Laboratories |
| TDG Sub-Committee | Transport of Dangerous Goods Sub-Committee |
| TSB | Triptic Soy Broth |
| UN | United Nations |
| UNTDG | *UN Model Regulations on the Transport of Dangerous Goods* (Orange Book) |
| UPU | Universal Postal Union |
| WHO | World Health Organization |

# 1. Introduction

As the incidence of infectious disease has expanded worldwide, the emergence of new pathogens (such as Nipah and SARS), the deadly permutations of existing pathogens (H5N1), and the reemergence of existing deadly diseases such as Ebola have had broader impacts on public health and security than ever before. In addition, following the "Amerithrax" attacks of October 2001, it has become exceedingly clear that the global biological threat extends beyond natural outbreaks of infectious disease: biological weapons (BW) may be used by terrorists to spread disease effectively among civilian populations. In the past, the spread of disease was often contained geographically by the more limited movement of humans and animals. The situation has changed. Infectious diseases may be most significant in third-world developing countries, but the vast global transportation network—by air, sea, and land—that has risen as a result of globalization also facilitates the spread of infectious disease as never before. Supporting this, a recent study has directly implicated air travel as a significant factor in the spread of human influenza.[1] Recognizing the growing threat, George W. Bush declared in November 2001 that "Infectious diseases make no distinctions among people and recognize no borders." Consequently, effective disease prevention and rapid medical response is more important than ever before.

While global transportation can contribute to the spread of disease, an efficient transportation system is also integral to the preventive measures and immediate public health response necessary to fight disease. Disease prevention includes measures that promote legitimate medical research and diagnostics, as well as decrease the risk that dangerous agents will be accidentally or intentionally released into the environment. International disease prevention, diagnostics, and medical response to outbreaks require safe, secure, and efficient transport of infectious substances (IS), whether naturally occurring or the result of a BW attack. The safe and secure transport of infectious substances must be efficient in order to quickly identify samples, provide evidence for attribution, and support decisions on international cooperation to address and contain the outbreak. Since biological materials are generally unstable and must be shipped on ice, air transport is the primary mode for transporting cultures, isolates, and diagnostic specimens.

Safe and secure packaging is crucial for the protection of people, property, and the environment. Concerns over the safety and security of current packaging for shipping IS sometimes interfere with the effective transport of important biological samples. The international response to the SARS outbreak was significantly hindered because many carriers refused to transport SARS specimens out of fear of inadequate packaging. Responses to bioterrorism events and advances in biomedical research also depend on safe and secure transport of IS. Often the most suitable laboratory or laboratories for testing the IS are located long distances away, and only a handful of laboratories

[1] Brownstein, J.S., *et al.*, "Empirical Evidence for the Effect of Airline Travel on Inter-Regional Influenza Spread in the United States," *PLoS Medicine*, 3. e401 (2006).

worldwide are equipped to diagnosis the most feared infectious diseases, such as foot-and-mouth disease, Ebola, and newly emergent agents such as the Nipah virus.

The self-remediating packaging technology developed by Sandia National Laboratories (SNL) was designed to improve the safety and security of IS transport, but should be effective against a whole range of hazardous materials. The packaging method will contain primary and secondary watertight containers just as the current packaging systems do. However, the new SNL-developed packaging system contains a novel decontaminating material that will kill or neutralize infectious organisms that may leak from the primary container. This self-decontaminating feature will lower the risk inherent to shipping IS, helping to alleviate the concerns of ground-based and air-based carriers. Thus, this fail-safe packaging technology will significantly enhance transport efficiency; reduce diagnostic and medical response time; and help prevent the accidental release or theft of pathogens.

## 1.1 Importance of Efficient Infectious Material Transfer

### 1.1.1 Economic Considerations

Every year, thousands of shipments containing hazardous materials are transported within the continental U.S. via all modes of transport. The sheer volume of these shipments shows that the efficient transport of hazardous materials is integral to the economic growth and prosperity of many different industries. The U.S. Department of Transportation characterizes hazardous materials based on the United Nations (UN) regulations described below as belonging to nine different hazard classes: Class 1 - Explosives, Class 2 - Gases, Class 3 - Flammable Liquids, Class 4 - Flammable Solids, Class 5 - Oxidizers and Organic Peroxides, *Class 6 - Toxic Materials and Infectious Substances*, Class 7 - Radioactive Materials, Class 8 - Corrosive Materials, and Class 9 - Miscellaneous Dangerous Goods. In 2002, the last year for which data from the Bureau of Transportation Statistics (BTS) were compiled, approximately 2,191,519 total tons of hazardous materials (valued at over $660 billion USD) were shipped within the U.S.—22.9% more than in 1997.[2] Of the transported tons, 8,459 were of Class 6 materials, a 32.9% increase over the total shipped in 1997. Importantly, because of industry coverage and shipment definitions in the BTS survey, some hazardous materials, including IS and radioactive waste, were not well represented in the data set, and the survey includes transport only within the continental U.S. Consequently, these figures underestimate the actual amounts of transported hazardous materials, particularly Class 6 IS.

### 1.1.2 Public Health and Research

The transport of infectious material—isolated pathogens or infected samples—is critical to the progress of scientific research and timely disease diagnosis. The scientific research community abides by a long-standing tradition and commitment to share information, materials, and reagents in order to advance science most effectively. The shipment of

[2] Bureau of Transportations Statistics 2002 Commodity Flow Survey Hazardous Materials, available at http://www.bts.gov/publications/commodity_flow_survey/2002/hazardous_materials/

infectious materials facilitates the discovery of new cures for debilitating diseases. In addition, infectious materials must also be transported quickly in emergency outbreak situations. Fast disease diagnosis is crucial for outbreak response and containment, ultimately preventing the spread of disease to more people or animals. Public health officials need to understand what disease they are working with, its biological properties, and how dangerous it is in order to know how to best control it. Often specialized diagnostic capacities, especially for very infectious and fatal diseases, are limited to just a few facilities, requiring that materials be sent for analysis. Samples collected from the field must be sent by road or air to clinical centers for diagnosis; many times the facilities are far enough away to necessitate air transport. It is critical in these situations that samples are sent as quickly and efficiently as possible, with as little delay as possible. In addition, most pathogens thrive at very specific physiological host conditions that must be maintained for growth and survival; even minor fluctuations can have a negative impact on viability. Absent these conditions, pathogens must be kept frozen or on ice to avoid loss in viability. Thus, shipment must be swift to avoid damage to the biological material caused by rapid thawing.

### 1.1.3 Safety and Security

Finally, there are safety and security concerns that make the rapid transfer of hazardous biological materials important. Generally, biological materials are most vulnerable during transport when they are no longer safely or securely contained within a laboratory. While in transit, they are susceptible to rough handling, being dropped, and other forms of physical abuse that could potentially cause packages to leak, exposing transport workers or civilian bystanders to possible illness. Lax containment and security also mean that packages are more vulnerable to theft. Numerous individuals may handle or have access to a package during transit—the more individuals with access, the more opportunities for the package to be stolen. Therefore, minimizing transit time will improve the safety and security of infectious agent transport.

## 1.2 Current Regulatory Environment and Standards

### 1.2.1 International Regulations

There is widespread consensus that the transport of hazardous materials can be dangerous because of the considerable risk that poorly packaged material can leak during transfer. A leak could potentially cause human casualties and require very expensive decontamination procedures for cleanup. From a shipping company's standpoint, negative shipping incidents involving hazardous materials warrant special concern because they could lead to negative publicity and a tarnished corporate reputation, possibly causing loss of business. Consequently, the movement and transport of hazardous biological materials has been subject to a variety of regulatory standards developed by international, national, and modal organizations. There is extensive overlap in the goals, approaches, and methods of the various standards. All the standards are similar in that they have been designed largely to protect transportation workers and the general public from the accidental release of hazardous materials during transport. These standards are well accepted in the industrialized world, but are much less institutionalized

in most developing third-world countries. More recently, as bioterrorism has become a larger issue, transport regulations have gradually incorporated more security provisions.

The United Nations Committee of Experts on the Transport of Dangerous Goods—a subsidiary body of the UN Economic and Social Council—has developed the standard international regulatory framework for the transport of hazardous materials. The committee has been dedicated to the creation and review of transport standards since the early 1950s; its primary mission is to create recommendations that promote the worldwide safe movement of hazardous materials by all modes of transport. The recommendations are formally published in the *UN Model Regulations on the Transport of Dangerous Goods* (UNTDG), which is commonly referred to as the "Orange Book" due to the color of the publication's cover. The first version was published in 1956. The United Nations Committee of Experts has appointed a Transport of Dangerous Goods Sub-Committee (TDG Sub-Committee) that is tasked with proposing updates to the Orange Book. The Sub-Committee is composed of 27 countries with voting status, as well as numerous nongovernmental agencies, such as the World Health Organization (WHO), with observer status.[3] The Sub-committee meets twice a year during odd-numbered years and once during the first half of even-numbered years to discuss policy amendments. The United Nations Committee of Experts meets during the second half of every even-numbered year to review and amend the Orange Book to keep it current. In December 2002, the Orange Book was amended to include security provisions that include clear recommendations for security awareness training and development of transport security plans. The revised edition was published in the summer of 2003.

While the recommendations of the Orange Book are nonbinding, they are designed to be used as a template to develop national legislation by the countries of the world. The book is drafted in a way that is meant to facilitate legislative adoption. The neutrality of the UN and the Orange Book's general ease of adoption have ensured that many countries have indeed based their national regulations for the transport of dangerous goods on the UN regulations. There are many advantages to global adoption of the Orange Book's regulations, most significantly the creation of a seamless global transport system that harmonizes the international transport of hazardous materials. Global adoption has the effect of lowering shipping costs because there is no need to comply with many different regulations. A global standard for packaging and shipping hazardous materials greatly facilitates cross-border and inter-modal shipments, negating the need for new packaging, classification, labeling, or paperwork when passing from one country to another or from one mode to another. International adoption of the UN regulations also decreases the possibility of safety noncompliance, enhances legal enforcement activities, and promotes more efficient trade and economic development. Without a standardized system for shipping dangerous goods, there would be a myriad of different regulatory frameworks, overly complicating the shipment of materials across borders.

The UN regulations are commonly accepted worldwide and serve as the foundation for most international, regional, national, and modal transport regulations. They are reflected

[3] The WHO acts as an important and very influential adviser in the formation of international transport regulations for infectious materials. The WHO publishes guidance on transport regulations.

in international law through international modal agreements put forth by transnational agencies such as the International Civil Aviation Organization (ICAO), the International Maritime Organization, the International Air Transport Association (IATA), and the Universal Postal Union (UPU). ICAO, a UN body, is responsible for harmonizing international air shipment standards. It reviews and typically adopts the Orange Book recommendations as the basis for its air-transport regulations, published as the *Technical Instructions for the Safe Transport of Dangerous Goods*. The ICAO regulations are legally binding and apply to all international flights. In addition, the IATA—a body that represents over 280 commercial airlines—develops industry standards for the transport of hazardous substances known as the *Dangerous Goods Regulations* (DGR). The DGR incorporates the UN Orange Book and ICAO provisions, and often includes further restrictions.

The civil aviation authorities of individual countries are responsible for developing national legislation that applies to flights within that country. Most national legislation typically adopts the UN and ICAO provisions, but some countries also apply additional regulations, requirements, and variations. State and carrier transport variations are normally published within the ICAO Technical Instructions, as well as in the IATA DGR.

### 1.2.2 U.S. Regulations

Within the Department of Transportation (DOT), the Research and Special Programs Administration is the principal body responsible for regulation regarding the safe and secure transport of hazardous materials within the U.S. DOT policy on the transport of hazardous substances is published in the *Hazardous Materials Regulations* (49 CFR Parts 100-180); the DOT adopted the UN system within the national Federal Code of Regulations for domestic transportation in 1980. Virtually all the hazardous materials transported within the U.S. comply with the international standards.[4] Many other U.S. government agencies are involved to varying extent in the regulation of domestic and international transport, including the Department of Commerce, Department of Homeland Security, the Department of Health and Human Services , the Department of Agriculture, the Federal Aviation Administration (FAA), the Federal Railroad Administration, the Federal Highway Administration , and the Coast Guard.[5]

## 1.3 Shipping Requirements

### 1.3.1 Classification

The UN Model Regulations define IS as "substances which are known or are reasonably expected to contain pathogens. Pathogens are defined as microorganisms (including bacteria, viruses, rickettsiae, parasites, fungi) and other agents such as prions, which cause disease in humans and animals."[6] IS are divided into two categories—Category A and Category B—for which different shipping requirements apply.

[4] U.S. Office of Hazardous Materials: http://hazmat.dot.gov/regs/intl/untdg.htm
[5] This list is not comprehensive.

Category A IS are defined as "An infectious substance which is transported in a form that, when exposure to it occurs, is capable of causing permanent disability, life-threatening or fatal disease in otherwise healthy humans or animals."[7] A list of examples, which includes organisms such as *Bacillus* anthracis, Ebola, and *Yersinia pestis*, is provided in the Model Regulations, but the list is not considered comprehensive. A certain degree of judgment is required on the part of the shipper. Category B IS are biological materials that fail to meet the criteria of Category A substances. They are still infectious, but are not considered very dangerous to human health. Diagnostic and clinical specimens are generally considered Category B substances.

Specific UN numbers and names must be assigned to dangerous goods before they are shipped, according to their hazard classification and their composition. Category A IS that cause disease in humans or both humans and animals are assigned the UN number UN 2814; the shipping name is "Infectious Substance, Affecting Humans." Substances that cause disease only in animals are assigned as UN 2900; "Infectious Substance, Affecting Animals." Category B substances are assigned as UN 3373 (except cultures, which are assigned as UN 2814 or UN 2900); "Diagnostic Specimens" or "Clinical Specimens." However, as of January 1, 2007, all Category B substances will be shipped as "Biological Substance, Category B."

### 1.3.2 Packaging

Since there are large differences in the danger posed by Category A and Category B substances, different shipping requirements—variations in packaging, labeling, and documentation—apply to each. For Category A substances, the packaging must meet United Nations Class 6.2 specifications and comply with the Packaging Instructions P620 delineated in the UNTDG. Category B substances must conform to P650 delineated in the UNTDG. It is the responsibility of the shipper to ensure that packages are prepared correctly with the appropriate boxes, and to ensure that the packages are marked and labeled correctly and accompanied with the proper shipping documents.

All international shipment of IS must be packed according to UN standards. A *triple-packaging system* should be used for both Category A and Category B materials. The basic characteristics of the triple-packaging system are the same for the two types of materials, but there are differences in package certification and durability requirements. In a triple-packaging system, the material to be shipped is placed in a securely closed, watertight, leak-proof, *primary* container that is carefully labeled. Enough *absorbent material* must be included immediately outside the primary container to completely absorb the contents in case of a spill. While the absorbent material prevents hazardous materials from leaking further, it is not designed for decontamination. The *primary* container must then be placed in a durable, watertight container that acts as a *secondary* container. The combined *primary* and *secondary* containers are then placed in an *outer*

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[6] Recommendations on the Transport of Dangerous Goods, Model Regulations, 13th revised edition, New York and Geneva, United Nations, 2003.
[7] *Ibid.*

*shipping* container constructed of fiberboard with suitable cushioning material that protects the contents from physical damage and water during transport. This triple-packaging system is shown in Figure 1.

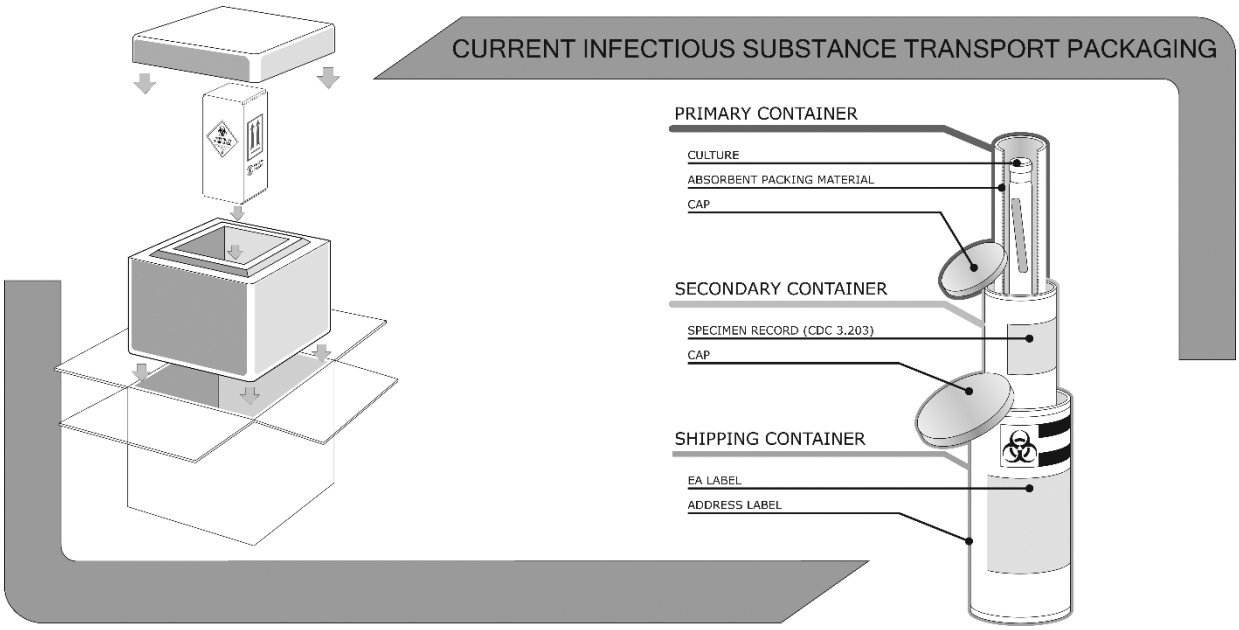


**Figure 1: Current Triple-Packaging System for Infectious Substances**

To ensure the performance of packaging used to ship Category A IS, triple-packaging systems must be certified according to a strict set of UN specifications. Certification requires that the wholly assembled packaging system pass a series of physical stress tests administered by an authorized entity. Performance tests include the following:

- Drop test – A package is dropped 9 meters onto its various surfaces (top, bottom, long and short sides, and a corner). The test must be conducted under wet and dry conditions; as well as after a period of time at -18 °C.
- Puncture test – A cylindrical steel rod is used to try to puncture the package.
- Internal pressure test – the package must withstand a pressure differential of at least 95 kPa applied hydraulically.
- Stacking test – The package must withstand force applied to the top surface by identical packages The minimum height of the stack is 3 m, including the test package.
- The package must be able to withstand temperatures in the range of -40 °C to +55 °C.

The tested package system is determined to be good if the primary receptacle does not release any of its contents. The UN packaging specification marking is applied to the packaging if it satisfactorily meets the durability testing criteria. Certified packaging systems can be purchased from a variety of authorized vendors online, although most of these suppliers are located in the developed world. Commercial carriers can also usually provide a list of local suppliers.

For Category B substances, the packaging has to be sturdy, and capable of withstanding the shocks normally encountered during handling and transport. The triple packaging should be capable of passing stress tests put forth by the UN, although these tests are not as strict or as physically damaging as the tests required for Category A transport. The whole package should be able to endure a 1.2 m drop, and the stacking and internal pressure tests described above. However, Category B packaging does not need to undergo a puncture test, testing documentation is not necessary, and UN approval marks are not used.

The amount of infectious material that can be legally shipped in a single package is limited. Currently, only 50 ml of liquid or 50 mg of solid Category A substances are allowed to be shipped in a single package on a passenger aircraft. Up to 4 liters or 4 kg per package are allowed on a cargo aircraft. For surface transport (by road, rail, and sea), up to 400 ml or 400 kg of Category A material is allowed in an outer shipping package. For Category B substances, up to 1 liter of liquid or 1 kg of solid can be put in a primary receptacle; the total volume of material in a single package cannot exceed 4 liters or 4 kg. There is no maximum package volume for surface transport of Category B material.

## 1.4 Current Packaging Problems

### 1.4.1 Hazardous Leaks

The triple-packaging system is designed to prevent the escape of infectious materials into the environment when a leak occurs, and not for decontamination. While there have not been any reported instances of illness that can be traced back to the accidental release of pathogens or toxins from shipped packages containing IS or diagnostic specimens, several instances have been reported where packages have been extensively damaged during transport.[8] Statistical data collected by a group of central laboratories worldwide indicate that an average of only 106 vials are broken per 4.92 million UN compliant packages (P650 and P620) shipped each year, showing that the current packaging guidelines are actually quite good at reducing shipping risk.[9] In each case, it appears that the leak was contained by the absorbent material, and secondary containers and outer packages remained intact. However, the absorbed biological material in these broken packages remained infectious and very dangerous to anyone who came in contact with it. Therefore, it is crucial that broken packages are detected quickly, and removed from the transport system by someone with hazmat training.

The data described above do not appear to include noncompliant packages. The triple-pack system is functional only as long as the person assembling the package has been properly trained and uses the correct packaging materials. In-depth training on the sometimes complicated shipping procedures is required for transport certification; this training is not readily available in many parts of the world. Without good training and

[8] World Health Organization, Transport of Infectious Substances (2004).
[9] *Ibid.*

packaging materials, the number of packages that break and release their contents into the environment can be expected to increase.

### 1.4.2 Carrier Refusal

Most packages containing IS are transported by air since the materials must arrive at their destination before the dry ice melts and the biological materials thaw. Any commercial carrier may refuse to transport any package if it appears to be improperly assembled or labeled, if it is not accompanied by the proper documentation, or if there is any suspicion whatsoever that the package may be hazardous. It is in the best interest of carriers to be cautious about what packages they transport since a negative incident could affect customer confidence in the company. Whether a carrier transports a package containing an infectious substance often depends on the pilot's perception of risk. There have been many incidents, particularly during disease outbreaks, when pilots have refused to transport biological specimens out of fear for their safety. Indeed, this occurred during the 2003 SARS outbreak when disease-response efforts were hindered after a number of carrier pilots refused to fly samples because of fear for their safety. The infectious specimens were in all likelihood assembled correctly and were safe, but transport was still delayed. Consequently, convincing pilots that a package is safe is a crucial factor in effectively transporting disease specimens.

### 1.4.3 Packaging Can Be Expensive

Although the UN Model Regulations have been adopted globally, there is often a level of noncompliance in the developing world that is very detrimental to safety. One reason for the noncompliance is that triple-packaging systems can be relatively expensive. The units come in many shapes and sizes that can be purchased from a number of local and international vendors. All the components of a Category A system are certified together as one unit; individual components from different units cannot be mixed and matched. The need to buy entire units to meet compliance is one reason for the expense. The quality, durability, and high degree of necessary testing add to the costs. Although the units can be reused—as long as they are in good condition—many laboratories in the developing world still cannot afford to purchase many of them. Proper triple-packaging systems are also not always readily available in some developing countries, further adding to the noncompliance.

## 1.5 Practical Application of Technology

The "fail-safe" self-remediating packaging developed by Sandia National Laboratories can improve the process by which IS are shipped in several ways described below.

### 1.5.1 Simplify Packaging Requirements and Decrease Prices

Since the self-remediating material is so effective at neutralizing a range of infectious agents, widespread application of the technology may help precipitate an easing of the current international, national, and modal transport restrictions and packaging requirements. Very quick decontamination at the source of any potential leak could

eliminate the need for the currently mandated triple-packaging systems in use today, which are designed for containment purposes only. Triple-packaging systems are relatively expensive, so use of this new decontamination technology could decrease global shipping prices markedly.

The new decontamination material may also decrease transport prices by enabling shippers to send more infectious material per package safely. The self-remediating material is effective enough at neutralization that it may be possible to send more than the currently allowed volume of Category A substances per package. A larger package volume limit would decrease prices sharply. However, further testing will be required to determine the true possibilities.

### 1.5.2 Decrease Shipping Risk

Numerous incidents occur yearly in which packages are damaged to the point where the IS leaks from the primary receptacle. The absorbent material present in the properly prepared packages soaks the contents up, but the material remains infectious, putting nearby individuals in danger. Quick detection of damaged, hazardous packages is critical to avoiding accidental infections. Application of the self-remediating technology described here would quickly neutralize any leaking IS, making it less important to detect broken packages quickly and decrease the chances of accidental infection and environmental contamination. The use of decontamination technology is also a practical way to decrease the perception of risk by carrier pilots and reduce the incidence of rejected packages and the associated shipping delays. IS packages that contain the self-remediating material would also be more secure, decreasing the chances that someone could illegitimately acquire potential BW material. The decontamination material will help prevent the malicious release of infectious material by initiating prompt inactivation of IS when the package is improperly accessed and tampered with.

# 2. Research Objectives and Methodology

The primary objective of this proposal is to develop a safe and secure packaging method for transport of IS that will meet the requirements for UN approval and alleviate the concern over leaking packages. The focus will be on the replacement of the current *absorbent material* in the triple-packaging system with a material that both *adsorbs and neutralizes* IS should a leak occur in the primary container. The adsorbent/neutralizing material will be based on the fundamental chemistry developed as part of the Sandia decon foam project where we developed a method to rapidly neutralize chemical and BW agents with a material with very low toxicity and corrosivity properties.[10] We envision the use of Sandia's decontamination technology in granulated (powdered) form in combination with highly absorptive material to absorb blood or other infectious materials leaked from a container. The IS would be contained within the absorptive material and subsequently neutralized.

We enhanced this triple-packaging system by the following:

- Developing a replacement for the absorbent material currently required for the IS triple-packaging method. This replacement material (based on Sandia DF-200 technology) will both absorb and neutralize any infectious material spilled from the primary container;
- Testing the efficacy of the neutralizing/adsorbent material against infectious material containing vegetative bacteria, viruses, and bacterial spores. The efficacy was demonstrated with infectious materials containing a high organic loading that is representative of blood or other bodily fluids;
- Identifying a method for pressure relief inside the secondary container to accommodate any gases released as a result of any degradation of the neutralizing material during shipment or reaction of the neutralizing material with the infectious material after a spill from the primary container;
- Testing the fail-safe packaging system to demonstrate that it will meet UN specifications for packages under both normal and extreme conditions.

This fail-safe packaging for shipping of IS should meet and improve upon the DOT and UN packaging specifications.

[10] http://www.sandia.gov/SandiaDecon/factsheets/TestResultsDec2003.pdf#search=%22df-200%22

# 3. Results

## 3.1 Constituents of Dry Decontamination Formulation

After considerable testing of the efficacy of a variety of formulations, the following two-part formulation was used. Part A contains a salt, a surfactant, a defoaming agent, and an oxidant activator. In our current formulation, we use potassium carbonate (62% by weight), Variquat 80 MC (16% by weight), Surfynol DF-62 (6% by weight), and diacetin (16% by weight). The first part is then encapsulated with a water soluble encapsulant. The size of the resulting encapsulated mixture can be controlled. Currently, we use polyethylene glycol (PEG) of various molecular weights as the encapsulant. The encapsulation is done using a hot-melt extrusion process and the encapsulated product has a diameter of about 3 mm. The PEG makes up about 78 wt% of the 3 mm bead.

Part B of the formulation is a solid oxidizing agent that has also been encapsulated. Currently, we are using sodium perborate monohydrate as the oxidizing agent and PEG of various molecular weights as the encapsulant, resulting in an encapsulated product with a diameter of about 3 mm. For Part B, the PEG makes up about 70% wt% of the 3 mm bead, although we also tested formulations with 90, 80, 60, and 50 wt% PEG and concluded that the 70 wt% performed most effectively.

## 3.2 Experimental

The E coli 11229 colonies were prepared by placing three cryo beads into 30 ml of Triptic Soy Broth (TSB). These were then incubated for 24 hours. At the end of that time, another 15 ml of TSB were added, and the culture was incubated for an additional 20 minutes. The broth was decanted leaving the beads, and 30 ml of Phophate Buffered Solution (PBS) were added.

To determine efficacy of the formulation in neutralizing E coli, we added 10 ml of the E coli suspension to each of four tubes. To the control tube, we added 1.35 g of DI $H_2O$, and to the other three tubes (replicates), we added 1 g of Part A of the decontamination formulation and 0.35 g or 0.175 g of Part B of the decontamination formulation. Samples were taken at 1 min, 5 min, and 30 min. Colony populations were counted on Triptic Soy Agar after being held at 37 °C for 24 hours.

## 3.3 Efficacy Testing

Using the efficacy testing procedure in Section 3.2, we counted populations of the control and the triplicate samples at times of 1, 5, and 30 min. Figure 2 using 0.35 g of Part B of the formulation and 1 g of Part A shows that the $\log_{10}$ of the Colony Forming Units/ml or log(CFU/ml) was essentially zero after each sample time, indicating that the formulation was effective in neutralizing the E coli essentially immediately.

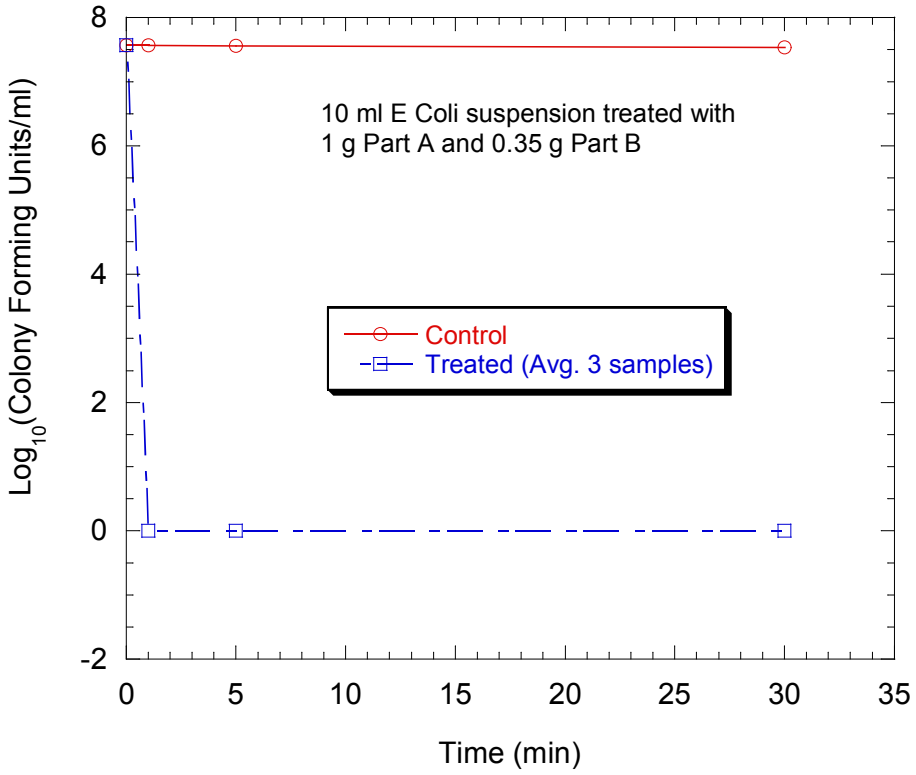


**Figure 2: Efficacy Testing with 1 g Part A and 0.35 g Part B**

Figure 3 shows the results with E coli treated with 1 g of Part A and 0.175 g of Part B. There were still CFUs at the 1 minute sample but essentially zero CFUs for the 5 and 30 minute samples. Thus, we concluded that the proper formulation for nearly immediate neutralization is 1 g of Part A and 0.35 g of Part B.

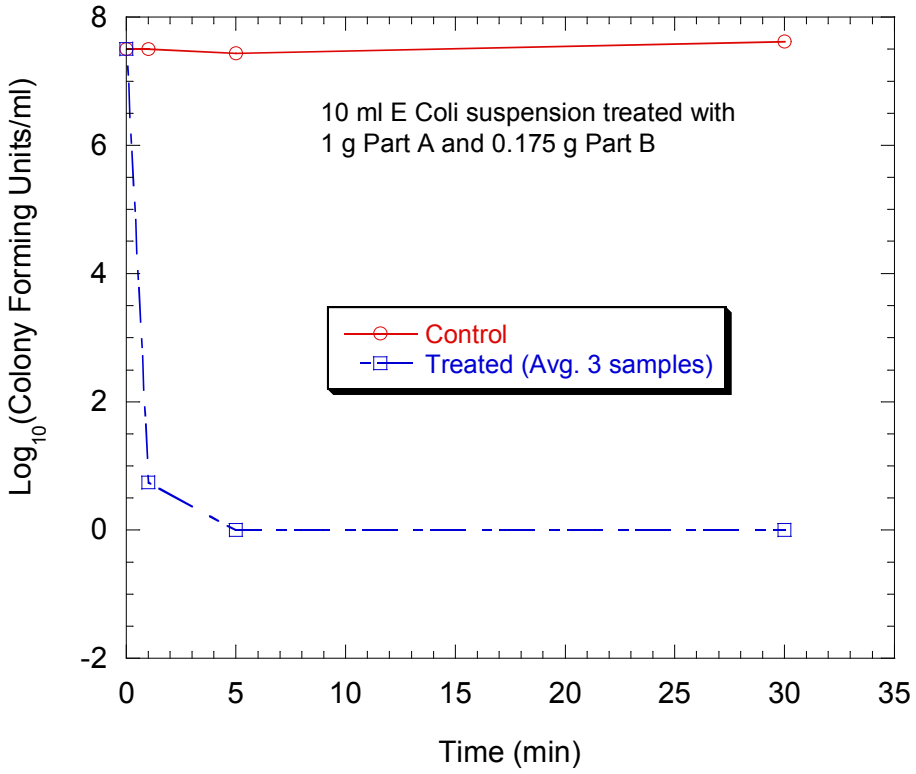


**Figure 3: Efficacy Testing with 1 g Part A and 0.175 g Part B**

## 3.4 Fail-Safe Packaging Prototype

A prototype that employed the neutralization/absorbent material was produced. As in the current triple-packaging system, the IS is placed inside of a leak-proof primary receptacle. The primary receptacle is in turn placed within a secondary container containing the Part A and Part B decontamination components, as depicted in Figure 4. The secondary container is designed to include one-way vents that allow excess gas to escape the container, while preventing gases from entering. This is important in the event that pressure builds up because of potential chemical reactions between leaking hazardous materials and the decontamination material. We have thus far used a watertight, sealable plastic bag with vents as the secondary container. The primary/secondary containers should then be packed within an outer box with cushioning material. Figure 5 shows an actual prototype. The jar in the pictures contains the neutralization/absorbent material that would normally be used to fill the secondary container (plastic bag). The primary container would then be placed within the filled bag; this packaging unit would then be placed within the outer box.

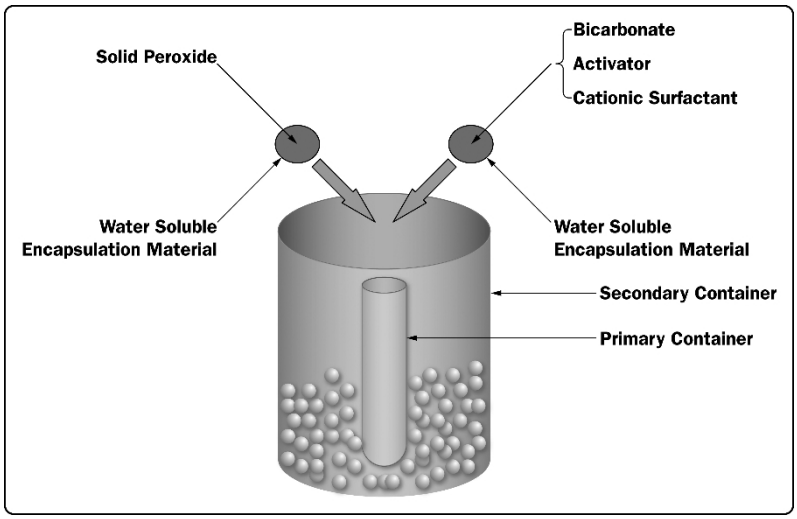


**Figure 4: Prototype Schematic**

**Figure 5: Fail-Safe Prototype Packaging**

# 4. Next Steps

## 4.1 Continue Testing

There are several immediate next steps regarding this fail-safe packaging technology. Before the packaging prototype can be applied to an actual transport environment, it first needs to be rigorously tested to ensure that it meets UN and DOT integrity requirements, and it must undergo reliability testing with pathogen surrogates to ensure that the material is capable of neutralizing leaking biological material consistently. Mechanical testing of the fail-safe packaging prototype will be carried out by an independent, certified laboratory. The packaging will be subjected to the proper drop, puncture, and pressure tests, as specified by the IATA manual. The stability of the absorbent/neutralization material will also be assessed during the stress tests to determine whether this material can be reused numerous times. Problems with the integrity of the material are not anticipated, and it is expected that the packaging will pass all UN and DOT requirements.

It will also be necessary to conduct efficacy testing using the complete fail-safe packaging prototype containing surrogate pathogenic material in a testing facility, ensuring that any biological materials that escape from the packaging are neutralized consistently and effectively. Liquids and diagnostic materials containing pathogen surrogates will be incorporated into fail-safe packages undergoing stress tests to see how well the system will work with live samples. If the packaging is deemed to be highly effective at the conclusion of the facility tests, preparations will then be made to test the fail-safe packaging in a limited, real-world transport system. Preliminary plans are being made to test the packaging in the transport of diagnostic specimens as part of an extensive disease surveillance system in Azerbaijan.

Finally, the absorbent/neutralization material will be laboratory tested to determine 1) whether larger volumes of IS can be safely shipped within single packages and 2) whether the material can effectively neutralize a variety of other hazardous substances such as noxious chemicals and corrosives.

## 4.2 Product Promotion

Concurrent with the various testing processes, it is critical to re-brief and update the international and U.S. agencies that have jurisdiction over global and domestic transport issues on the testing progress and the potential uses of the prototype in real-life scenarios. We will also begin to develop strategies for introducing the packaging into appropriate markets. The WHO will be briefed, as well as various U.S. government entities, including the DOT and the FAA, and trade organizations such as the Air Transport Association (ATA).

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