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Handle with Care

UN3373 compliance is becoming increasingly crucial with the globalisation of the pharmaceutical industry. Shipping of biological, and sometimes infectious, substances across borders must be stringently regulated

Sue Fletcher at Alpha Laboratories Ltd

Catizone states, "When you are in the business of creating lifesaving drugs, the mundane detail of shipping logistics is not usually the first concern that springs to mind.

"The biopharmaceutical industry, by its very nature, is one in which underlying business operations are often perceived as secondary to the higher calling of treating or even curing some of the most devastating diseases on earth. But ensuring that clinical samples reach their destination safely, securely, and at the right temperature is just as crucial as any element of the drug discovery process (1)."

Medical laboratory and clinical personnel have always needed to transport biological samples from the patient source, between clinics and laboratories for centralised testing in clinical trials. However, a growing number of trial projects are now being performed on a global scale, with activity significantly increasing in developing countries, particularly Asian and Latin American locations (2).

This provides economic and participant recruitment benefits. Additionally, data can be collected from varied populations to support licence applications that require geographically different trial sites to ensure the product is safe and works in the same way in varying ethnic groups. This requirement is true for both pharmaceutical companies working on the next blockbuster drug and for not-for-profit partnerships developing a new drug or vaccine for a neglected disease. Thus, organisational, scientific and regulatory factors combine to encourage the globalisation of clinical trials.

When a central lab is used for analysing critical specimens in a global programme, they must be shipped across national borders. This brings logistical and increasingly complex challenges for the safe, punctual and compliant transport of patient samples. While blood, urine, microbiological and viral sampling has always been common, more tissue samples are being collected as biomarkers and for repositories (3). The regulations governing the transportation of infectious and diagnostic substances are also becoming ever more stringent. Ignorance towards the latest requirements and procedures could lead to noncompliance. This has potentially catastrophic consequences for clinical trial programmes, with delays in receipt of samples and even the risk of prosecution of the staff responsible for the packaging (4).

Sample Types

Biological samples fall under the Dangerous Goods Regulations because they may contain pathogens. The transportation of dangerous goods is strictly regulated, and it is a legal and mandatory requirement to comply with the regulations when transporting human or animal samples. The aim of the regulations is to enable these

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goods to be transported relatively easily, in a consistent, recognisable manner. This ensures that all such parcels and their contents reach their destination in good condition, while not endangering the environment or anyone who comes into contact with them during their journey. However, how often do you receive specimens that are inadequately packaged?

The general guideline from the WHO is that samples – such as blood, tissue, excreta, secreta etc. From humans or animals – that are not assigned to Category A, Infectious Substances, are considered to be Category B, Biological Substances. These samples are then assigned to UN3373 and must be packaged according to the International Air Transport Association's (IATA) Dangerous Goods Regulation or the European agreement concerning the International Carriage of Dangerous Goods by Road (ADR) Packing Instruction 650 for transport.

There is a third category that is not generally used, but often causes the most confusion. Samples described as "has minimal likelihood that pathogens are present" can be classified as exempt (5). Many think that exemption means that no special packaging is required, but this is not the case. Exempt samples also require a three layer packaging system to be compliant with legislation.

Costly Consequences

The results of noncompliance can be expensive. For the trial, this could mean delays in receipt of samples, loss of data and costs to repeat the patient tests. For lab staff, it could result in additional workload for clean-ups and re-tests. For courier staff, handling the package during transit could cause ill health and time off work. For the lab, incorrect packaging could result in fines, and, in the worst case scenario, the person who packaged the sample could be jailed. Ultimately, the individual responsible for the parcel is the person who packaged it.

Assess Your Sample

Under the Dangerous Goods Regulations, nine classes of goods are segregated according to the particular risks they pose.

Human or Animal Specimens fall into Class 6 – Toxic and Infectious Substances

6.1 – Toxic Substances
6.2 – Infectious Substances, where these types of samples are assigned

Category A
Pathogens vary greatly in their ability to cause disease and how dangerous they can be. Dependent on their mode of infection, and the format in which the sample is shipped – eg, culture or natural samples, pathogens that are capable of causing permanent disability or life-threatening or fatal disease in humans or animals that were otherwise healthy prior to exposure – are categorised as Category A Infectious Substance. A complete list of these organisms is contained within the regulations, but can change with each update.

Transport of Category A, Infectious substances is strictly regulated and must only be done in UN-approved packaging.

Category B
Most pathogens fall into Category B Biological Substances as they may cause disease or illness, but it is not usually too serious.

Category B has less stringent requirements, but, nevertheless, the packaging instruction detailed in the regulations must be adhered to. The majority of samples transported around the globe fall under UN3373 Biological Substances [Category B].

Exempt Samples
Under Class 6.2, a third subdivision causes a great deal of misunderstanding, and these are exempt samples. Many people think that 'exempt' means you do not require any special packaging, but this is not the case. Exempt samples are described as those that have "minimal likelihood that pathogens are present".

However, the authorities in some countries believe that, unless you are able to categorically say that the sample does not contain pathogens, it should be treated as any other sample containing pathogens. Even when a sample is categorised as 'exempt', it still requires a triple layer packaging system to be compliant with the Dangerous Goods Regulations.

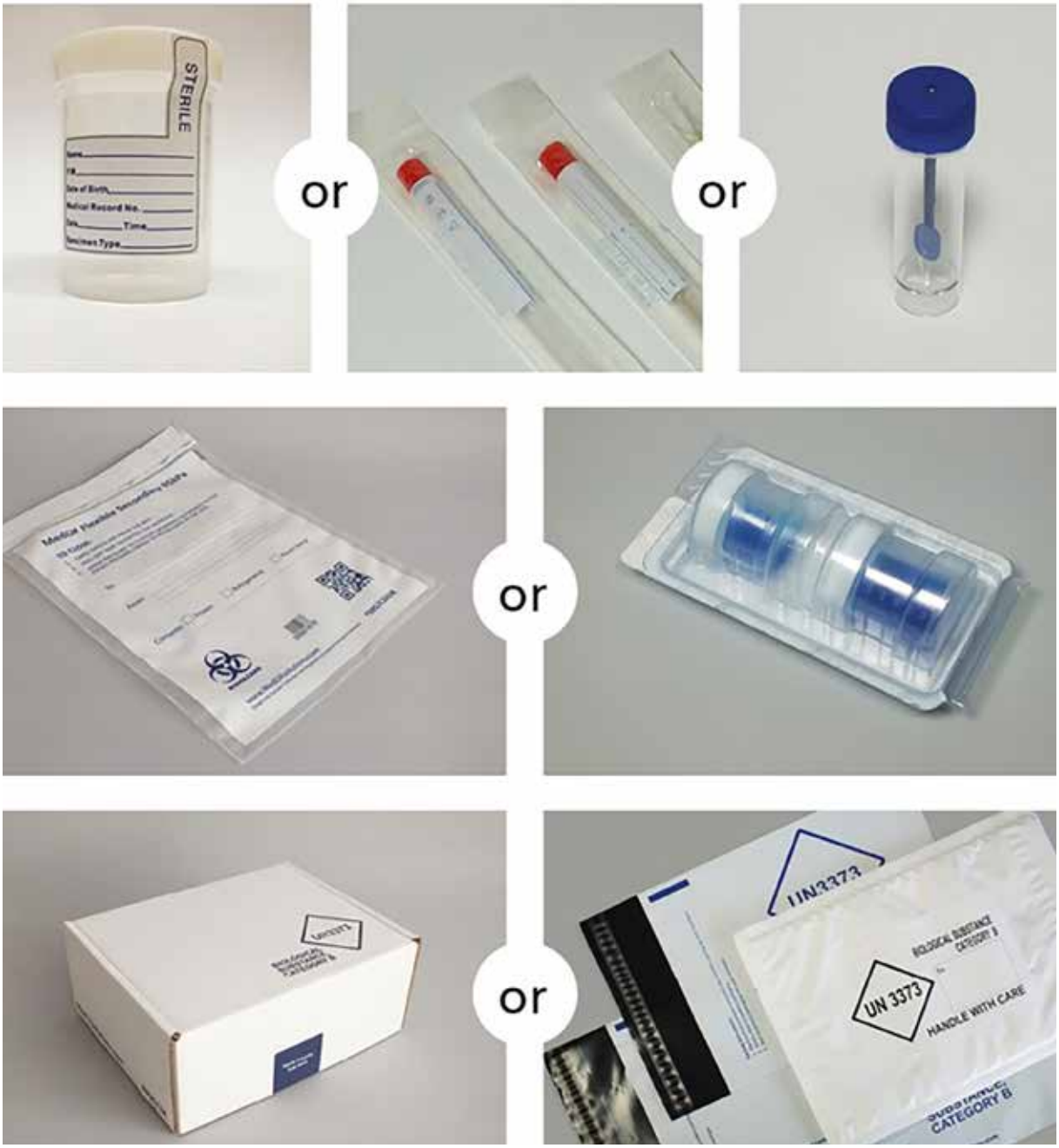

Figure 1: Basic three component requirements

Lab personnel are trained to handle human or animal samples correctly to keep themselves and others safe. However, when it comes to sample transport, the legislation can be difficult to interpret and costly to implement, both in terms of time and money.

Minimum Requirements

When samples are being sent as Category B, the packaging has to meet certain minimum conditions. Principally, it must consist of three components: the leak-proof primary receptacle (blood tube/universal container), a secondary packaging (sealed plastic bag or rigid container) plus an outer packaging (cardboard box or mailing envelope) (see Figure 1).

For ADR, the primary or secondary packaging must pass the 95kPa pressure differential test conducted at an ambient temperature. The entire package, with its three layers, must withstand a 1.2m drop test without any damage to the primary container, and either the secondary or outer layer of packaging must be rigid. Additionally, sufficient absorbent material must also be included in the package to absorb all of the sample volume (eg special absorbent sheet, blue roll, foam, cotton wool).

> **Trying to meet these requirements using standard materials around the lab can be a daunting task and lead to variability within the packaging processes**

Figure 2: UN3373 Labelling

When sending multiple samples in one package, each primary container must be individually wrapped or separated so they do not contact each other directly. Samples being sent under UN3373 Category B, Biological Substance should also display the appropriate symbol. This is a diamond in a colour, that contrasts clearly with the package background and must be accompanied by the correct shipping name, which is "Biological Substance, Category B". The diamond should contain 'UN3373' in letters at least 6mm high (see Figure 2).

Additional stipulations and requirements particularly relate to the IATA. The same 95kPa pressure differential test applies, but the container, whether primary or secondary, must pass this test at both -40°C and 55°C. Maximum volume (1L) and weight (1Kg) limits apply to the primary and outer container (4L or 4Kg). The outer packaging layer must be rigid and contain an itemised list of contents. The UN3373 diamond symbol must be at least 50mm along each side of the diamond shape, and the outer packaging must be at least 100mm x 100mm in size.

Trying to meet these requirements using standard materials around the lab can be a daunting task and lead to variability within the packaging processes. For example, the use of various absorbent materials could mean insufficient absorbency is provided or excess padding is added, which makes the package unnecessarily bulky and more expensive to mail. Ideally, DIY solutions should be avoided as there are specific tests regarding robustness and absorbency that elements of the packaging must comply with to be considered suitable.

To help provide some packaging consistency, a range of off-the-shelf materials are readily available. Some innovative solutions are available that provide quick and convenient ways to meet the regulations while minimising transport costs. It is important to shop around to find the most appropriate and cost-effective solution for your particular requirements.

References

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About the author

Sue Fletcher is a BSc Hons graduate with a number of years' experience working in research labs. Having attained the necessary standard on a Civil Aviation Authority-Approved course, Sue is certified in the Carriage of Diagnostic and Infectious Substances by Air and provides advice and training seminars across the country on UN3373 Dangerous Goods Packaging.

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