HEALTH SURVEILLANCE MANUAL ON TRANSPORTATION OF HUMAN BIOLOGICAL MATERIAL FOR CLINICAL DIAGNOSIS PURPOSES

National Health Surveillance Agency - ANVISA

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National Health Surveillance Agency (Anvisa)

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CONFIDENTIAL

ABNT Brazilian Standards Association Techniques

ADR European Agreement Concerning the International Carriage of Dangerous Goods by Road

ANAC National Civil Aviation Agency

ANTAQ National Transport Agency waterways

ANTT National Transport Agency Terrestrial

AWB Air Waybill

CNPJ National Register of Legal Entities

CPF Individual registration

CT-e Electronic Shipping Knowledge

DGD Dangerous Goods Declaration

DGR Dangerous Goods Regulation

IT'S THE Operating Specifications

EPC Collective Protection Equipment

EPI Individual protection equipment

HBV Hepatitis B virus

HCV Hepatitis C virus

HIV Acquired Immunodeficiency Virus

THERE IT IS International Association of Air Transport

INMETRO National Institute of Metrology, Quality and Technology

NOTOC Notification to Commander

OACI Civil Aviation Organization International

WHO World Health Organization

HIM-HER-IT United Nations Organization

PI Packing Instruction

POP Standard operational procedure

ground floor Resolution of the Collegiate Board

RID Regulations Concerning the International Transport of Dangerous Goods by Rail

SNVS National Health Surveillance System

SOLAS Safety of Life at Sea

A United Nations

UPU Universal Postal Union

1. INTRODUCTION

The transport of clinical samples is part of the pre-analytical phase of the operational process of performing laboratory tests. A large laboratory processes around four samples from 5,000 patients/day, transporting around 20,000 biological samples daily. For the laboratory to offer reliable results, it is not enough for the techniques to be performed correctly and with trained personnel: it is necessary to use a properly preserved biological sample. An adequate biological sample is understood to be one obtained in sufficient quantity, in an appropriate container, well identified and transported in order to maintain the integrity of the material to be researched.

Technological advances in the diagnostics segment have directed laboratories towards the optimization and concentration of processes, with the use of increasingly sophisticated equipment and the use of a large logistics network composed of transporters who need guarantee reliability, punctuality and regularity to the activities of transit of biological samples.

This manual aims to define health surveillance guidelines for the transport of biological samples of human origin for clinical diagnosis purposes.

Compliance with the requirements established by the standards aims to reduce the possibility of contamination of the samples as a result of exposure to infectious microorganisms that can escape from the packaging due to breakage, leakage or inadequate packaging during the transport process, in addition to guaranteeing the integrity and stability of the packaging. transported biological material.

These guidelines apply to all sender, carrier, recipient and other actors involved in the process of transporting biological material. In the case of transporting samples for clinical diagnosis, the general settings are presented in Table 1.

Table 1 - General settings for the transport process of clinical samples for laboratory diagnosis. Brazil, 2014.

Sender	Conveyor	recipient
Health service	Own transport (own load)	Health Service
Health service	Own transport + passenger and cargo carrier	Health Service
Health service	Outsourced transport (commercial)	Health Service
Health service	Outsourced transport + passenger and cargo carrier	Health Service
Health Service	Transport by state institutions authorized by the Ministry of Health/ Health's Secretary	Health Service

This manual is based on the requirements defined by the Resolution of the Collegiate Board of Directors (RDC) 20/2014 of the National Health Surveillance Agency (Anvisa), which regulates the activities of transporting clinical samples from the point of view of health surveillance, establishing the rules for the sending health services, in general clinical laboratories, can carry out these transport activities to another health service, which may be another clinical laboratory, hospitals, clinics or similar, using infrastructure for their own transport logistics or contracting third parties. Norms from other regulatory bodies in the transport sector were also used, such as the National Civil Aviation Agency (Anac), the National Land Transport Agency (ANTT), the National Traffic Council (Contran) and others.

The clinical laboratory may use the information in this publication also for guidance, as appropriate, for the transport of biological samples as hand luggage made directly by the individual, from his/her residence to the laboratory, in a private or public vehicle, in order to guarantee the safety and quality of the process.

The content of this manual is based on national and international technical and legal references and therefore its application should not, at any time, represent an obstacle to the implementation of policies or the development of practices related to new technologies. For information purposes only, the publication describes concepts and models that can help senders, recipients and transporters to comply with the legal requirements demanded by current regulations. Thus, this manual has educational purposes to reduce information asymmetry, clarify doubts or disseminate guidelines related to routines and procedures for compliance with legislation, it is not

aimed at expanding or restricting technical or administrative requirements already established by the rules in force.
It also intends to help health surveillance agents in the understanding and conceptual harmonization of regulatory requirements, in order to contribute to the inspection process.

Most biological material transport activities in Brazil involve the routine transit of samples between laboratories, hospitals, clinics and research centers. Those involved in this complex transport process will find in this manual basic guidelines on classification, packaging, labeling and regulatory procedures for the transport of biological material.

In this way, it is expected to contribute so that laboratory services comply with the requirements defined by Brazilian legislation and, at the same time, that the agents of the National Health Surveillance System (SNVS) can count on one more technical reference that helps them to perform their duties. functions to achieve its mission in the face of health risk.

2. DEFINITIONS

For the purposes of this manual, the following definitions are adopted:

I - Packaging of biological material: procedure for packaging biological material for the purpose of transport, aiming at protecting the material, people and the environment during all stages of transport to its final destination. It should be noted that packaging is essential to ensure the conservation of the material's biological properties and must be standardized through validated processes.

II - Patient samples: those collected directly from human beings, including (but not limited to) excretion, secretion, blood and its components, tissue and fluid samples, and body parts to be transported for research, diagnostic, research, treatment and prevention of diseases.

III - Baggage: term used in air transport as an asset belonging to the passenger or crew, carried on board an aircraft, under a contract with the carrier.

IV - Checked Baggage: term used in air transport as baggage that is transported in the hold of a aircraft.

Accompanied Baggage: when carried on the same aircraft as the passenger to which it belongs. In this manual, the term “accompanied baggage” was also used in relation to land transport.

Unaccompanied Baggage: when the owner is not on board the aircraft, but the baggage has been checked in as cargo. In this manual, this term has also been used in relation to land transport.

V - Hand luggage: term used in air transport as luggage carried by the passenger on board an aircraft. In this manual, the term “hand luggage” was also used in relation to land transport.

VI - Recipient: any legal entity, public or private, responsible for receiving the transported biological material.

VII - Specimens or samples for diagnosis: any biological material of human or animal origin, including – but not limited to – waste, secretions, blood and its components, tissues or fluids shipped for diagnostic purposes. This material, depending on professional judgment, may be classified as a Category A infectious substance, a Category B biological substance, a minimal risk human specimen or an exempt biological material.

VIII - Label: identification affixed to the label, without erasures and that does not compromise the original words of the label. The label is produced later and its function is to complement the words on the label throughout the transport process.

IX - Absorbent material: any inert material that has the property of absorbing, absorbing or sucking free liquid substances, such as cotton, paper, fabric, foams and others.

X - Human biological material: tissue or fluid constituting the human organism, such as excrements, body fluids, cells, tissues, organs or other fluids of human origin or isolated from them. These microorganisms are not considered hazardous materials if they are unlikely to cause disease in people or animals. They are considered infectious substances, therefore hazardous materials, if, through exposure to them, they are capable of spreading disease.

XI - Refrigerant material: material or substance capable of maintaining the biological material at a previously specified temperature range during the transport process, such as ice, recyclable ice, dry ice and liquid nitrogen.

XII - Mode of transport: mechanism, alternative or type of transport vehicle used in the displacement of human biological material.

XIII - UN or ONU number: number composed of four digits, preceded by the letters UN or ONU, determined by the United Nations for the identification of dangerous substances or of a particular group of substances.

XIV - Transport process: activities and procedures defined with the purpose of transporting biological material from a sender to one or more recipients by means of a carrier. The map of the transport process begins with the intention to transport, with the due agreements and documentation procedures. Then comes the phase of packaging the material in an appropriate container, its dispatch and accommodation in the transport vehicle and the transit itself, its transshipment from the vehicle (withdrawal from the transport container of the transport vehicle), its delivery to the recipient and, finally, the final disposal of biological material in an appropriate place in the recipient service. Temporary storage, when applicable, is part of the transport process.

XV - Sender: any legal entity, of a public or private nature, responsible for preparing and sending human biological material to a recipient, by means of a mode of transport. Also known as shipper or shipper, the sender is responsible for packaging the clinical samples. The laboratory must define a qualified professional responsible for the packaging activity, who has technical knowledge about the biological samples to be transported.

XVI - Labeling: procedure for labeling, marking and labeling packages intended for the transport of human biological material.

XVII - Label: corresponds to the printed or lithographed identification and to the words painted or engraved by fire, pressure or self-adhesive, applied directly on containers, packages, envelopes, envelopes, cartridges and any other packaging protector, and cannot be removed or altered during the transport and storage.

XVIII - Carrier: individual or legal entity that transports biological material from a sender to a specific recipient, including commercial, public or private carriers, and those carrying their own cargo.

Own transport: the service (clinical laboratory) that transports clinical samples for diagnosis, using its own vehicles and/or personnel.

Commercial carrier: the service (clinical laboratory) that hires an outsourced carrier, public or private, by means of a contract, agreement, term of commitment or other similar documents, to carry out activities related to the transport of clinical samples.

Passenger and cargo carrier: collective transport company, that is, that transports individuals and their cargo in specific compartments in the road, rail and waterway modes, as well as air operators.
In these vehicles, in certain previously agreed situations and with defined responsibilities, it is possible to transport loads (biological material) unattended.

XIX - Validation: sets of actions used to prove that operational procedures, processes, activities or systems produce the expected result. Validation exercises are normally conducted according to previously defined and approved protocols that describe tests and acceptance criteria.

XX - Technical Transport Supervisor: professional trained and formally appointed to carry out the activities of implementation, execution and monitoring of the transport processes of biological material. It may be of higher or technical level designated by the clinical laboratory or by the outsourced transport company that has the technical capacity to intervene in the phases of the transport process under its supervision.

3. REGULATORY FOUNDATIONS APPLICABLE TO THE TRANSPORT OF BIOLOGICAL MATERIAL

Safety, as well as success in the transport process, will only be achieved through the fulfillment of responsibilities on the part of the sender, the carrier, the recipient and the others involved.

Regulatory guidelines for the transport of biological materials have their origins in the Recommendations of the United Nations Expert Committee on the Transport of Hazardous Materials, a committee of the Economic and Social Council of the United Nations (UN).

Some international standards were fundamental for defining the regulatory requirements adopted in Brazil, serving as a basis for the preparation of this manual, namely:

- Guidance on Regulations for the Transport of Infectious Substances – World Organization for Health (WHO);
- Letter Post Manual – Universal Postal Union (UPU);
- Regulations Concerning the International Carriage of Dangerous Goods by Rail (RID) – União Europeia;
- European Agreement Concerning the International Carriage of Dangerous Goods by Road (ADR);
- Technical Instructions for the Safe Transport of Dangerous Goods by Air – Aviation Organization International Civil (ICAO);
- Dangerous Goods Regulations (DGR) – Association International Air Transport (IATA);
- International Maritime Dangerous Goods Code – International Convention for the Safety of Life at Sea (Solas).

The main objective of these standards is safety against biological risk during the transport process, in order to ensure that the population and workers involved are protected from exposure to any infectious agent linked to the transported cargo.

In Brazil, the transport of biological samples is regulated by several agencies, according to the route used. A brief description of the main rules for transporting biological material in the country follows. This list does not cover all the standards in the area, and is only intended to provide guidance to interested parties.

Ground transportation

- Law 9,503, of September 23, 1997, and its updates. Establishes the Brazilian Traffic Code (http://www.planalto.gov.br/ ccivil_03 / leis / l9503.htm).

National Land Transport Agency - ANTT (http://www.antt.gov.br)

- Resolution 420, of February 12, 2004, and its updates. Approves the Supplementary Instructions to the Regulation of Land Transport of Dangerous Goods (http://www.antt.gov.br/index. php/content/view/1420/Resolucao_420.html).
- Resolution 3665 of May 4, 2011 and its updates. Updates the Regulation for Road Transport of Dangerous Goods, approved by Decree 96.044, of May 18, 1988 (http://www.antt.gov.br/html/objects/ _ downloadblob.php?cod_blob=6096).

Air Transport

National Civil Aviation Agency – Anac (http://www.anac.gov.br)

- Brazilian Civil Aviation Regulation (RBAC) 175 – Transport of Dangerous Goods in Civil Aircraft (http://www2.anac.gov.br/ transparency/pdf/RBAC%20175.pdf).
- Supplementary Instruction (IS) 175-00A, of April 3, 2014. Guidance on procedures for shipping and transporting biological and infectious substances on civil aircraft (http://www2.anac. gov.br/biblioteca/ IS/2014 / S175-004A.pdf).

Water transportation

National Agency for Waterway Transport – Antaq (http:// www.antaq.gov.br)

- Resolution 2,239, of September 15, 2011, which approves the standard of procedures for the safe transport of dangerous products through port facilities located inside or outside the organized port area (http://www.antaq.gov.br/portal /pdf/ System/Publication/0000004425.pdf).

postal service

Mail

- Law 6,538, of June 22, 1978. Provides for Postal Services (http://www.planalto.gov.br/ ccivil_03 / leis / L6538.htm).

Brazil is a signatory to the international agreement Letter Post Manual (2009), organized by the Universal Postal Union, which defines the parameters for the transport by post of biological samples and infectious substances.

Brazilian Association of Technical Standards - ABNT

- ABNT NBR 7500:2013. Identification for land transport, handling, movement and storage of products.
- ABNT NBR 15481:2013. Road transport of dangerous goods — Minimum safety requirements.
- ABNT NBR 7501:2011. Land transport of dangerous goods — Terminology.
- ABNT NBR 9735:2014. Set of equipment for emergencies in land transport of dangerous goods.
- ABNT NBR 14785:2002. Clinical laboratory - Security requirements.

sanitary regulations

The health regulations that deal with the transport of biological samples for clinical diagnosis are intended to add to the existing regulations in the field of transport the concern with risk management in the conservation of biological characteristics. These standards generally contain the principles established by the WHO, defined in the Transport of Infectious Substances Regulations (http://apps.who.int/iris/bitstream/10665/78075/1/ WHO_HSE_GCR_2012.12_eng.pdf).

The following are the main sanitary regulations that, in some way, deal with the transport of biological samples for clinical diagnosis:

- **Ordinance GM 472, of March 9, 2009:** approves, in its annex, the Mercosur technical regulation for the transport of substances infectious diseases and biological samples within the scope of Mercosur member countries.

- **RDC 302, of October 13, 2005:** defines that the clinical laboratory and the collection point must have written instructions for the transport of patient samples, establishing deadlines, temperature conditions and technical standards to guarantee their integrity and stability. Thus, according to the characteristics of the biological material to be transported, it is the responsibility of the laboratory to guarantee the quality of the sample to be analyzed.

- **RDC 61, of December 1, 2009:** provides for the operation of Histocompatibility and Immunogenetics Laboratories that carry out activities for the purpose of transplantation and other measures, and deals with the transport of biological samples from the collection site to the analysis laboratory.

- For the importation of human biological material for diagnostic purposes, **RDC 81, of November 5, 2008,** which provides for the Technical Regulation of Imported Goods and Products for Health Surveillance, must be followed.

- **RDC 20, of April 10, 2014:** provides for the sanitary regulation for the transport of human biological material, with the objective of defining and establishing sanitary standards for the transport of biological material in its different modalities and forms. This standard is applied to senders, transporters and recipients of biological materials of human origin related to services and products under sanitary surveillance. It defines human biological material as tissue or fluid constituting the human organism, such as excrements, body fluids, cells, tissues, organs or other fluids of human origin or isolated from them. It is worth noting that RDC 20/2014 is a sanitary surveillance standard with the objective of defining and establishing sanitary standards for the transport of biological material, without prejudice to the provisions of other current norms peculiar to each material and mode of transport, to guarantee the safety, minimize health risks and preserve the integrity of the transported material. In this way, RDC 20/2014 does not overlap with other transport standards, on the contrary, since the aforementioned standard

from Anvisa refers to the particularities of the norms referring to the transport of biological material in each mode of transport. When using the land mode, the ANTT requirements must be followed, as well as air (Anac) and waterway (Antaq) transport, complemented by the health requirements of RDC 20/2014.

4. RISK CLASSIFICATION IN THE TRANSPORT OF BIOLOGICAL MATERIAL

The risk classification of biological material for transport is a WHO recommendation, addressed to governments and international organizations concerned with the regulation of the transport of dangerous goods. The WHO's objective is to provide a set of basic rules that can be used in national and international regulations for the various modes of transport, in order to standardize understanding on this matter, with sufficient flexibility, however, to accommodate special needs that may arise.

According to the WHO, biohazard assessment for transport should be based on the following principles:

1. The usual precautions in the handling of biological material were originally developed for health services, with the objective of reducing the risk of transmission of infectious agents, from sources of known, suspected or unknown dangers, through the use of protective barriers. Precautions apply to blood, other body fluids, secretions, excretions (except sweat), non-intact skin and mucous membranes. Health service workers use individual and collective barriers (Individual Protection Equipment - PPE and Collective Protection Equipment - EPC) for their protection and to protect patients, materials and the environment.

And how is the protection/barrier in the transport of biological material?

In transport, the protective barrier is the packaging system.

2. Infectious mechanisms explain the factors that must be taken into account when assessing the risk of infection by a specific pathogen.

Among them are:

- The stability of the agent in the environment.
- The agent exposure mode.
- The pathogenicity of the agent and the infectious dose.
- The natural and artificial way of infection.
- Preventive and/or therapeutic treatment.

Bloodborne agents, such as hepatitis B virus (HBV), acquired human immunodeficiency virus (HIV), and hepatitis C virus (HCV), are effective in infecting hosts through mechanical injection of infected material, contact with non-intact skin (with wounds, cuts, burns, etc.), through sexual intercourse and others.

During transport, the exposure of individuals to these pathogens can probably occur in the case of accidents with extravasation of infectious material, during cleaning procedures of this material without adopting appropriate protection and safety measures, and during biological material packaging procedures, in that the professional is directly exposed to the hazards involved. The transit of properly conditioned (packaged) biological material can be considered a safe activity.

The dose or number of infectious agents needed to initiate an infection depends on virulence and the gateway to the host; for example, HBV needs 10 viral particles in the mechanical injection mechanism, influenza A virus needs 800 viral particles per nasopharyngeal inoculation, and it takes about 110 *Vibrio cholerae* per ingestion to cause cholera infection (WHO, 2004). . Of course, these data are related to experimental conditions, but it is correct to say that the higher the concentration of the infectious agent, the greater the chance of infections, without taking into account all the immunological defense mechanisms of the individuals.

HAZARDS are inherent to infectious agents.
RISKS can be managed

For transport purposes, infectious or infectious substances are understood to mean biological materials that are known or reasonably suspected to contain pathogens, that is, to contain pathogens or are reasonably suspected of containing them. Pathogens are microorganisms (such as bacteria, viruses, *rickettsiae,* parasites, and fungi) and other agents, such as prions, that can cause disease in animals and humans.

Biological risk in transport should be understood as the level of risk from exposure to biological agents during transport processes. This risk must be evaluated by the pathogenesis, mode and relative ease of transmission through biological materials, and also by the

disease reversibility due to the availability of known and effective preventive treatments, considering the mechanisms of barriers to contact with biological material during transport activity, such as packaging systems, defined compartments in vehicles, personnel training and others.

The WHO considers dangerous goods to be those that present risks during transport. There are nine classes of dangerous goods. Three of them are important for the transport of biological material:

Class 2: Gases

Division 2.2 - Risk Subclass

Non-flammable and non-toxic

Example: liquid nitrogen.

Class 6: Toxic and infectious substances

Division 6.2 - Infectious substance

Category A infectious substance

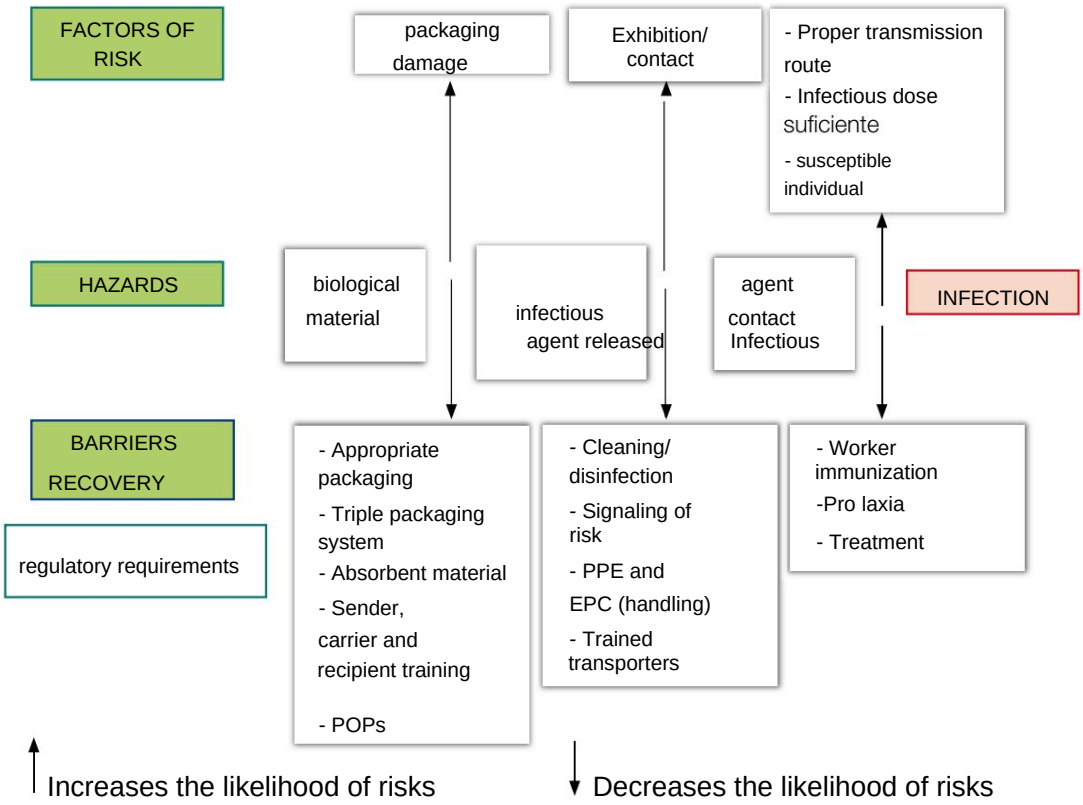
Category B biological substance

Class 9: Miscellaneous of dangerous goods

Eg: dry ice.

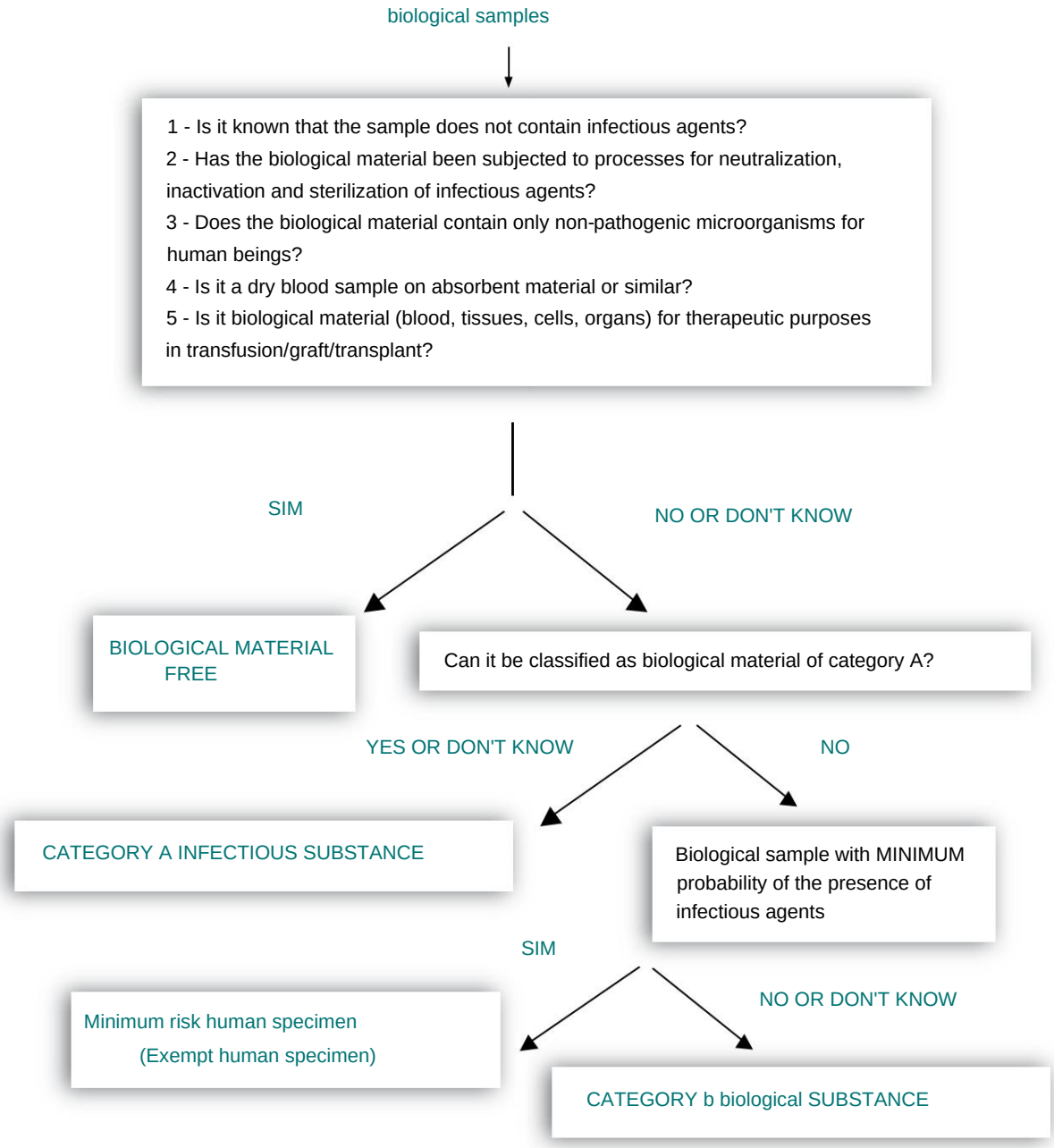
In Figure 1 it is possible to demonstrate the configuration defined in RDC 20/2014 to establish control items in the transport of biological material, with a focus on reducing biological risk.

Figure 1 - Biological risk management in the transport of biological material.



Source: Anvisa, 2014.

Figure 2 - Risk classification flowchart applied to the transport of biological material.



Source: WHO. 2013-2014 Transport of Infectious Substances Regulatory Guidelines (adapted).

Attention! The requirements defined for each classification of biological material described below are determined in the rules of Anac (Supplementary Instruction IS 175-00A, of April 3, 2014) and of ANTT (Resolution 420, of February 12, 2004; Resolution 3665, of May 4, 2011).

5. CATEGORY A INFECTIOUS SUBSTANCE

It is an infectious substance (infectious biological material) that is transported in such a way that, when exposed to it, an infection can occur that results in permanent disability, life threatening to humans or previously healthy animals.

There are several examples that fit this category, such as biological materials with Ebola virus or culture media with *Bacillus anthracis.*

Appropriate names for infectious biological materials are:

UN 2814: infectious substance affecting humans, in Portuguese, or *infectious substance affecting humans,* in English.

UN 2900: infectious substance affecting animals only, in Portuguese, or *infectious substance affecting animals only,* in English.

Attention! Category A biological substances are considered high-consequence **hazardous goods** that could potentially be used in a terrorist incident and, as a result, produce serious harm, such as accidents or mass destruction. It should be remembered that exposure occurs when an infectious substance is released from the packaging, resulting in physical contact with humans or animals.

The classification of biological samples in UN 2814 or UN 2900 must be based on the known clinical history of the individual (human or animal nature) of origin of the material, on signs and symptoms, on local epidemiological conditions, according to the judgment of a qualified professional recognition of the risk factors in question.

This classification applies to all modes of transport: air, land and water. Transporting infectious hazardous material requires special care and specific requirements, depending on the mode of transport used.

Below is a list prepared by the WHO with examples of microorganisms identified and classified in category A. This list is not exhaustive. It is recommended to include in this category new or emerging pathogens that meet these same criteria and also those samples of substances that it is not known whether or not they meet these criteria.

Table 2 - Pathogenic agents present in infectious substances of category A.

UN number and proper name for transport	microorganisms
UN 2814 Infectious substances that affect human beings	*Bacillus anthracis* (cultures only)
	Brucella abortus (cultures only)
	Brucella melitensis (cultures only)
	Brucella suis (crops only)
	Burkholderia mallei (Pseudomonas mallei) – glanders (crops only)
	Burkholderia pseudomallei - Pseudomonas pseudomallei (crops only)
	Chlamydia psittaci – avian strains (cultures only)
	Clostridium botulinum (cultures only)
	Coccidioides immitis (cultures only)
	Coxiella burnetii (cultures only)
	Congo-Crimean hemorrhagic fever virus
	Dengue virus (cultures only)
	Eastern equine encephalitis virus (cultures only)
	Escherichia coli, verotoxigenic (cultures only)
	Ebola virus
	Flexal Virus
	Francisella tularensis (cultures only)

continues

UN number and proper name for transport	microorganisms
UN 2814 Infectious substances that affect human beings	Guaranite Virus
	Vírus Hantaan
	Hantaviruses causing hemorrhagic fever with renal syndrome
	Hendra virus
	Hepatitis B virus (cultures only)
	Herpes B virus (cultures only)
	Human immunodeficiency virus (cultures only)
	Highly pathogenic avian influenza virus (cultures only)
	Japanese encephalitis virus (cultures only)
	Vírus Junin
	Kyasanur forest disease virus
	Lassa virus
	Machupo Virus
	Virus Marburg
	simian smallpox virus
	Mycobacterium tuberculosis (cultures only)
	Nipah virus
	Omsk hemorrhagic fever virus
	Polio virus (cultures only)
	Rabies virus (cultures only)
	Rickettsia prowazekii (cultures only)
	Rickettsia rickettsii (cultures only)
	Rift Valley Fever Virus (Cultures only)
	Russian spring-summer encephalitis virus (cultures only)
	Mockingbird Virus
	Shigella dysenteriae type 1 (cultures only)
	Tick-borne encephalitis virus (cultures only)
	smallpox virus
	Venezuelan equine encephalitis virus (cultures only)
	West Nile Virus (Cultures only)
	Yellow fever virus (cultures only)
	Yersinia pestis (crops only)
UN 2900 Infectious substances that affect only animals	African swine fever virus (cultures only)
	avian paramyxovirus type 1 - velogenic disease virus of Newcastle (crops only)
	Classical swine fever virus (cultures only)
	Foot-and-mouth disease virus (cultures only)
	Nodular dermatosis virus (cultures only)
	Mycoplasma mycoides - contagious bovine pleuropneumonia (cultures only)
	Small ruminant plague virus (crops only)
	Rinderpest virus (crops only)
	Sheeppox virus (cultures only)
	Goat pox virus (cultures only)
	Swine vesicular disease virus (cultures only)
	Vesicular stomatitis virus (cultures only)

Source: WHO. 2013-2014 Transport of Infectious Substances Regulatory Guidelines.

Names in italics described in Table 2 are bacteria, mycoplasmas, rickettsiae or fungi.

Cultures are incubated biological samples (for the purpose of pathogen multiplication/growth); clinical samples are collected directly from humans or animals. This difference is important for the classification of infectious substances, which will affect the choice of packaging.

5.1. Packaging, labeling and labeling

For the transport of biological materials classified as category A, detailed guidelines must be requested from the transport regulatory bodies on how to proceed with the proper packaging (packaging) of these materials.

It is not necessary to display the technical names (name of the microorganism in question) on the outer packaging.

Symbol: three crescent crescents superimposed in a circle.

Risk label or label: Category A infectious substance label

The bottom of the label must contain the term **Infectious Substance,** followed by the phrase **In case of damage or leaks immediately notify the public health authority.**

note about risk label

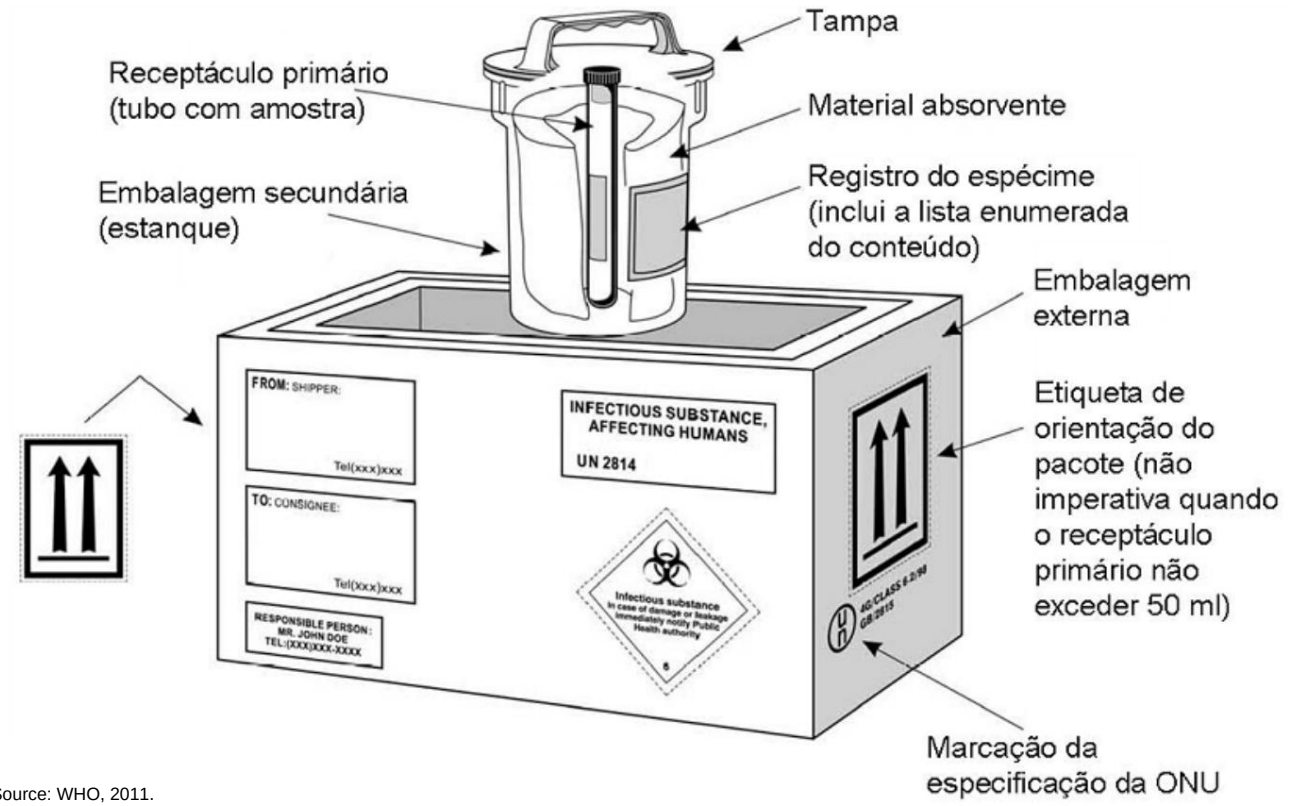
Dimension: diamond with at least 100 mm x 100 mm.
It is accepted that each side has a length of at least 50 mm (smaller packages).

Inscriptions: black color.

Background: white. Number “6” in the lower corner.

Description: Infectious substance – In case of damage or leakage, notify public health authority immediately.

Figure 3 - Schematic packaging model for category A.



Source: WHO, 2011.

The packages must contain the markings and information required by current legislation, namely:

- Sender's name and address.
- Name and address of recipient.
- Name and telephone number of the responsible person (who must be on standby 24 hours a day until the shipment arrives). This person must be able to provide technical information about the transported biological material.
- Correct designation of the consignment (proper name for transport: infectious substance that affects humans).
- UN numerical code (UN 2814).
- Approved packaging mark (Anac)/certified (Inmetro – ANTT).
- Orientation arrows (only mandatory when the primary packaging contains more than 50 ml).

For air carriers

Category A infectious substances shall not be loaded onto an aircraft in the same compartment as animals, food, feed or other edible substances intended for human or animal consumption, except when the Category A infectious sample, animals and food are loaded in separate cargo devices, and when not adjacent to each other if stored on board the aircraft. Air operators must be aware of this requirement, which is subject to inspection by Anac.

The maximum amount of infectious samples in the category The one contained in a single outer packaging permitted in air transport, excluding the weight of ice, dry ice or liquid nitrogen used to refrigerate the samples, is:

a) 50 ml or 50 g for passenger aircraft and their cargo; and

b) 4 l or 4 kg for cargo aircraft.

Passengers and crew may not carry Category A biological samples in hand luggage,

checked-in or on-body baggage. These must be shipped separately as cargo, in order to be segregated. It is noteworthy that only air transport operators that have authorization to transport dangerous goods in their Operating Specifications (EO) can transport them.

Anac establishes that the packaging for the transport of dangerous goods must be approved by the Agency. Companies producing packaging for transporting infectious materials of category A by air must arrange for the certification of their packaging in accordance with a quality control program.

For ground carriers

During transport and at loading, unloading and transhipment locations, infectious Category A samples must be kept isolated/separated from foodstuffs and other products for human or animal consumption.

Several rules applied to land vehicles must be followed, such as the placement of safety panels on the outside, risk labels on vehicles and equipment with tachograph. During transit, the carrier must carry an emergency card and emergency kit (basic PPE – gloves and helmet), in addition to other requirements that must be consulted with ANTT.

For land transport of infectious materials of category A (UN 2814 or 2900), the packages must be certified, that is, have authorization to use the Inmetro seal of conformity, according to ANTT standards and Inmetro Ordinance 326/2006.

Packing Instruction 620 – Packing Instruction 620 (PI 620) contains information on packaging details for Category A infectious material applied to all modes of transport.

There is no list of packaging suppliers that comply with Packaging Instruction 620. However, an internet search using a search engine often provides adequate information and access to national regulations. Searching for expressions such as “UN packaging” and “UN packaging of infectious substances” and other keywords can help in identifying requirements and suppliers of these authorized packaging. Shipping companies must be able to provide details of local suppliers of these packages to shippers and recipients.

The following requirements and packaging characteristics are defined in Packaging Instruction 620, described in Anac and ANTT standards.

5.2. Packing Instruction 620 (PI 620)

- This instruction is applicable to UN (UN) numbers 2814 and 2900.

- Packages that meet the legal technical requirements and that have been approved are authorized, consisting of a system consisting of three components (primary container(s), secondary packaging and rigid outer packaging), as described below:

a) Inner packaging that includes:

(i) leakproof primary container(s)
leaks;

(ii) a leak-proof secondary packaging
leaks;

(iii) except for solid infectious substances, absorbent material in sufficient quantity to absorb the entire contents, placed between the primary container(s) and the secondary packaging;

(iv) if the secondary packaging contains multiple fragile primary containers (eg glass), these must be individually wrapped to avoid contact between them.

b) A rigid outer packaging with adequate strength for its capacity, mass and use and whose smallest external dimension is at least 100 mm.

additional requirements

1) Inner packagings containing infectious substances shall not be consolidated with others containing products of types unrelated to such biological materials. Complete volumes can be over-packed according to

with the legal technical provisions; such overpack may contain dry ice.

2) Except in the case of exceptional shipments, such as whole organs that require special packaging, the following additional requirements apply:

a) Lyophilized substances: the primary containers must be heat-sealed glass ampoules or glass vials with rubber stoppers equipped with metal seals or other devices that ensure sealing.

b) Liquid or solid substances:

(i) *substances shipped at ambient temperature or above.* Primary containers must be glass, metal or plastic. A means must be adopted to guarantee a watertight seal, for example, heat sealing (thermal seal), stopper with coating or seamed aluminum seal. If threaded caps are used, they must be reinforced with adhesive tape, with paraffin sealing tape or with closing latches;

(ii) *substances shipped chilled or frozen.*
Ice, dry ice or other refrigerant must be placed around the secondary packaging, alternatively, in an overpack with one or more complete volumes, marked according to technical standards. There must be interior supports to hold the secondary packaging and the packages must be added in a safe transport position after the ice or dry ice has dissipated. If ice is used, the outer packaging or overpack must be watertight. If dry ice is used, the outer packaging or overwrap must allow carbon dioxide gas to escape. The primary container and secondary packaging must maintain their integrity at the temperature of the refrigerant used;

(iii) *substances shipped in liquid nitrogen.*
Primary plastic containers capable of withstanding very low temperatures must be used.
The secondary packaging must also be able to withstand very low temperatures and, in most cases, must fit over each primary container individually. Provisions for the transport of liquid nitrogen must be met. The primary container and secondary packaging must maintain their integrity at the temperature of liquid nitrogen.

3) Whatever the temperature of the shipment, the primary container and secondary packaging must be able to withstand, without leakage, an internal pressure that produces a pressure differential of at least 95 kPa and temperatures in the range of -40ºC to +55ºC .

4) The ability of a package to withstand without leakage an internal pressure that produces the specified pressure differential shall be determined by testing samples of primary containers or secondary packages. The appropriate test method must be selected based on the type of container or packaging. Acceptable test methods include any method that produces the required pressure differential between the inside and outside of a primary container or secondary package. Testing can be performed using internal hydraulic or pneumatic pressures or external vacuum test methods. Internal hydraulic or pneumatic pressures can be applied in most cases, as the required pressure differential can be achieved in most circumstances.

An external vacuum test is not acceptable if the specified pressure differential is not achieved and maintained. External vacuum testing is a generally acceptable method for rigid containers and packaging, but is not normally acceptable for a) flexible containers and flexible packagings or b) filled and closed containers and packagings under an absolute atmospheric pressure of less than 95 kPa.

5) Other dangerous goods shall not be packed in the same packaging as those belonging to Division 6.2 Infectious Substances, unless they are necessary to preserve, stabilize, prevent their degradation or neutralize their hazards.

6) Shippers/shippers of infectious substances must ensure that packages are prepared in such a way that they arrive at their destination in good condition and do not present danger to people or animals during transport.

7) A detailed list of contents must be placed between the secondary packaging and the outer packaging.

8) When the infectious substances to be transported are unknown, but it is suspected that they meet the criteria for inclusion in category A, the term “infectious substance suspected of belonging to category A”, in Portuguese, or *suspected category A infectious substance,* in English, must be shown in parentheses after the appropriate transport name.

9) Before an empty package is returned to the sender or sent to another location, it must be

disinfected or sterilized to eliminate any danger.
Any label or marking indicating that it contained an infectious substance must be removed or discarded.

5.3. Documentation

The consignor and/or carrier of Category A infectious material must complete specific documents and forms related to the dangerous articles/products that will be required for shipment/dispatch of this type of material.

For **land transport (ANTT standards),** the documents must contain:

- Full address of recipient and name and telephone number of a person responsible for technical information on biological material.
- Information that identifies the vehicle or mode of transport to be used, the date of transport and the name of the airports, transfer stations and unloading locations.
- Appropriate warnings, when necessary, such as: “Keep cool between +2°C and +4°C” or “Keep frozen” or “Do not freeze” or other warnings.

For **air transport (ANAC standards),** the documents must contain:

- Electronic Bill of Lading (CT e) for domestic transport or Air Waybill (AWB) for international transport.
- Declaration of the Consignor of Dangerous Goods (Dangerous Goods Declaration – DGD).
- Notification to Commander (Notification to Captain – Notoc);
- Detailed list of contents placed between secondary packaging and outer packaging.
- Original Certificate of Conformity in the packaging, issued by the manufacturer.
- Anac's approval document, for national packages, or a package document approved by another civil aviation authority or competent body for such approval, for imported packages.

For documentation purposes, the appropriate transport name (infectious substance that affects humans) must be accompanied by the technical name (microorganism identification) in parentheses.

Anvisa recommendations!

5.4. care in transport

The sender must handle the biological material with the care required by the type of risk involved, as well as carry personal protective equipment and have collective protective equipment. Further guidance should be requested from the competent health authorities (sanitary surveillance and epidemiological surveillance), in order to comply with the requirements of Good Laboratory Practices with high-risk biological materials.

Carriers and their personnel must be trained to understand all regulations regarding the packaging, labeling, transport and transport documentation of infectious substances. If the carrier finds any errors in the labeling or documentation, it must immediately notify the sender or consignee so that appropriate corrective measures can be taken.

In case of accidents, leaks or other damages that expose infectious material during transport, the person responsible for transport must:

a) avoid handling the volumes or handle them as little as possible;

b) inspect adjacent volumes for contamination and separate those that may have been contaminated;

c) inform the competent local authority about the spill and the possibility of contamination of people along the route. In this case, public security authorities can be called immediately (police, fire brigade, civil defense, among others);

d) request technical-sanitary information from the sanitary surveillance and epidemiological surveillance bodies on how to deal with certain biological materials with high-risk infectious agents and the need for initial measures for the individual quarantine of people, loads and vehicles;

e) notify the consignor and consignee. The sender (shipper) is the person indicated for more information about the risks involved in contact with such biological material.

The recipient must have a suitable place for receiving and opening the packages. The degree of isolation must be proportionate to the risk level of the substances.

Before an empty package is returned to the sender or shipped to another location, it must be thoroughly disinfected or sterilized and any labels or marks indicating that it contained an infectious substance must be removed or erased.

Anvisa recommendations!

5.5. Particularities of the transport of SUBSTANCES DA category A

Transporting Category A infectious substances requires coordinated action between the shipper, carrier and recipient to ensure the safety and timely delivery of these substances in good condition. To this end, the following measures must be taken:

a) prior understanding between the sender, the carrier and the recipient. The shipment of infectious substances will not be carried out without prior agreement between the shipper and the recipient;

b) in order to guarantee the unhindered operation, it is necessary to prepare all shipping documents, in strict compliance with the rules governing the transport of dangerous goods (Class 6 - Subdivision 6.2);

c) whichever mode of transport is used, transit must be carried out by the fastest possible route. If transshipment is necessary, precautions must be taken to ensure that there is special care, rapid handling and monitoring of materials in transit;

d) the sender must notify the recipient in advance of the transport details, such as mode of transport, flight or train number, tax document number and expected date and time for the arrival at destination so that the shipment can be promptly received. The fastest means of communication must be used for this notification.

Infectious substances of this nature can only be shipped, in case of importation, after the recipient has assured, with Anvisa, that such biological substances can be legally imported. Likewise, for exporting this type of material, it is important to ensure, with the health authority of the recipient country, of the necessary requirements for this type of transport.

For air transport, it is worth remembering that not all airlines are allowed to transport category A substances. Therefore, you should contact Anac to verify this situation.

6. CATEGORY B BIOLOGICAL SUBSTANCE

The requirements indicated below are defined by Anac and ANTT.

It is an infectious or potentially infectious biological material that does not meet the criteria for inclusion in category A.

Category B includes samples for clinical diagnosis that are known or suspected to contain infectious agents causing disease in humans, such as samples from patients suspected of being infected with pathogenic microorganisms or samples known to be positive/reactive.

It is worth mentioning that even samples positive for HIV and HBV are classified in category B, except when it is material in the culture medium of these viruses, which is then classified as category A (see Table 1 of this manual).

Attention! Cultures that aim to reproduce microbiological agents can be classified as category A or B, depending on the microorganism cultivated.

The vast majority of biological samples transported in patient diagnostic laboratory services can be classified as category B, with the exception of blood samples dried on absorbent paper and other situations in which

a qualified healthcare professional ensures that samples to be transported have the least likely risk of causing infection during the transport process if contact with the material occurs.

6.1. Packaging, labeling and labeling

Biological material classified in this category must be marked UN 3373.

Proper shipping name for samples classified as UN 3373: “biological substance category B”, in Portuguese, or *biological substance category* B, in English. By land transport regulations, the name “diagnostic specimens” is still accepted .

The UN 3373 mark must be displayed on the surface of the outer packaging, on a contrasting color background, and must be clearly visible and legible. The mark must be in the form of a square fixed at an angle of 45° (lozenge-shaped), each side being at least 50 mm long; the line width must be at least 2 mm and the letters and numbers must be at least 6 mm high.

THERE IS NO RISK LABEL APPLICABLE TO THE SUBSTANCE BIOLOGICAL CATEGORY B A 3373

For the transport of biological substance of category B (UN 3373), the current normative provisions referring to Packaging Instruction 650 (Packing Instruction – PI 650) must be applied.

The requirements of PI 650 are found in international standards and internalized in Brazil by transport regulatory agencies (Anac, ANTT and Antaq).

6.2. Packing Instruction 650 (PI 650)

6.2.1. general provisions

Biological samples for diagnosis must be packaged in good quality packaging, which must be strong enough to withstand the impacts and loads normally encountered during transport, including transshipment and storage, as well as subsequent manual or mechanical handling.

Packages must be constructed and closed in such a way as to prevent any loss of content that may be caused under normal conditions of transport, by the action of vibration, or by changes in temperature, humidity or pressure.

The packaging system must consist of three components:

a) primary packaging(s): containers that come into direct contact with the biological material; can be manufactured with glass, plastic, metal and others. Eg: collection tubes;

b) secondary packaging, capable of enveloping and containing the primary packaging(s).
It can consist of plastic bag, plastic *bag,* PVC box, metal and others;

c) external packaging: containers with adequate rigidity. It can be made of cardboard, PVC, metal and others. In land transport, one of the packages – secondary or external – must be rigid.
For air transport, the outer packaging must be rigid.

Primary containers must be packed in secondary packaging so that, under normal conditions of transport, they cannot break or be punctured, nor that their contents can leak.

Secondary packaging must be secured in outer packaging. Any leakage of the contents of the primary packaging must not substantially impair the protective properties of the outer packaging. For air transport, secondary packaging must be packed in rigid outer packaging. Depending on the configuration of the packaging system, cushioning materials may be used. These cushioning materials can be any type of device used during packaging to ensure that the primary packaging will be firm and secure to withstand movement during transport.

It should be noted that the secondary packaging must be made of appropriate material and arranged in such a way as to ensure that, in case of leakage of the contents of the primary packaging, there will be no leakage into the external packaging and other elements that make up the packaging system.

The types of materials that make up the packaging, both external and internal (secondary and primary), are affected by agents such as temperature, humidity and pressure. The performance of cardboard or similar materials, for example, can be quickly affected by moisture; plastics can become brittle at low temperatures; and the performance of other materials, such as metals, is unaffected by either humidity or temperature.

6.2.2. some features

of the tests carried out with

PI 650 packaging

Base test: the packaging system must successfully pass the free fall test at a height not less than 1.2 m and a puncture test. After the drop test, there must be no leakage from the primary containers, which must remain protected by absorbent material, in the case of liquid samples, in the secondary packaging. After the puncture test, the primary packaging must remain intact.

- When the outer packaging is made of cardboard, the packaging system to be tested must be subjected to water spraying that simulates an atmospheric precipitation (rain) of approximately 5 cm per hour, for at least one hour. After this procedure, the package must be subjected to the free fall and perforation test.
- When one of the packages is made of plastic, the packaging system must be conditioned in an atmosphere of -18ºC or less, for a minimum period of 24 hours and, within 15 minutes after its removal from this atmosphere, it must be submitted to the test free fall and perforation. When the test atmosphere contains dry ice, the conditioning period can be reduced to four hours.
- If the packaging system has dry ice as a refrigerant, regardless of the type of material constituting the packaging, it must be stored until all the dry ice has dissipated and then it can be subjected to the free fall and puncture test.

6.2.3. Features not

sample packaging

liquids

The primary packaging(s) must be watertight and must not contain more than 1 liter, in the case of air transport. This amount excludes ice, dry ice, or liquid nitrogen used to keep samples cool.

Secondary packaging must be watertight.

If several fragile primary containers, such as glass tubes, are placed together in a single secondary package, they must be individually secured or separated to avoid contact with each other.

When the primary packaging is sufficiently resistant (plastic tubes), however, in normal transport situations and with the necessary characteristics of tolerance to pressure and temperature variation, they can be transported together, without the need for individual separation.

The absorbent material must be placed between the primary container(s) and the secondary packaging. The amount of absorbent material must be sufficient to absorb the entire contents of the primary container(s), so that any leakage of the liquid substance does not compromise the integrity of the outer packaging.

The primary container or secondary packaging must be capable of withstanding, without leakage, an internal pressure, producing a pressure differential of not less than 95 kPa

(0.95 bar). Attention should be paid to extreme temperatures (–40ºC to +55ºC).

The entire packaging system must not contain more than 4 liters. This amount excludes ice, dry ice, or liquid nitrogen used to keep samples cool.

6.2.4. Peculiarities not case of solid samples

The primary packaging(s) must be resistant to material loss. In air transport, the packaging system must not exceed the limit of 4 kg, except in cases containing body parts, organs or whole bodies.

Secondary packaging must be resistant to material loss.

If several fragile primary containers, such as glass tubes, are placed together in a single secondary package, they must be individually wrapped or separated to avoid contact with each other. This requirement does not apply when heavy-duty plastic collection tubes are used.

If there is any doubt as to whether there is residual liquid in the primary packaging during transport, suitable packaging for the liquids, including absorbent materials, must be used.

6.2.5. Peculiarities not case of chilled samples

Chilled or frozen samples using ice, dry ice and liquid nitrogen

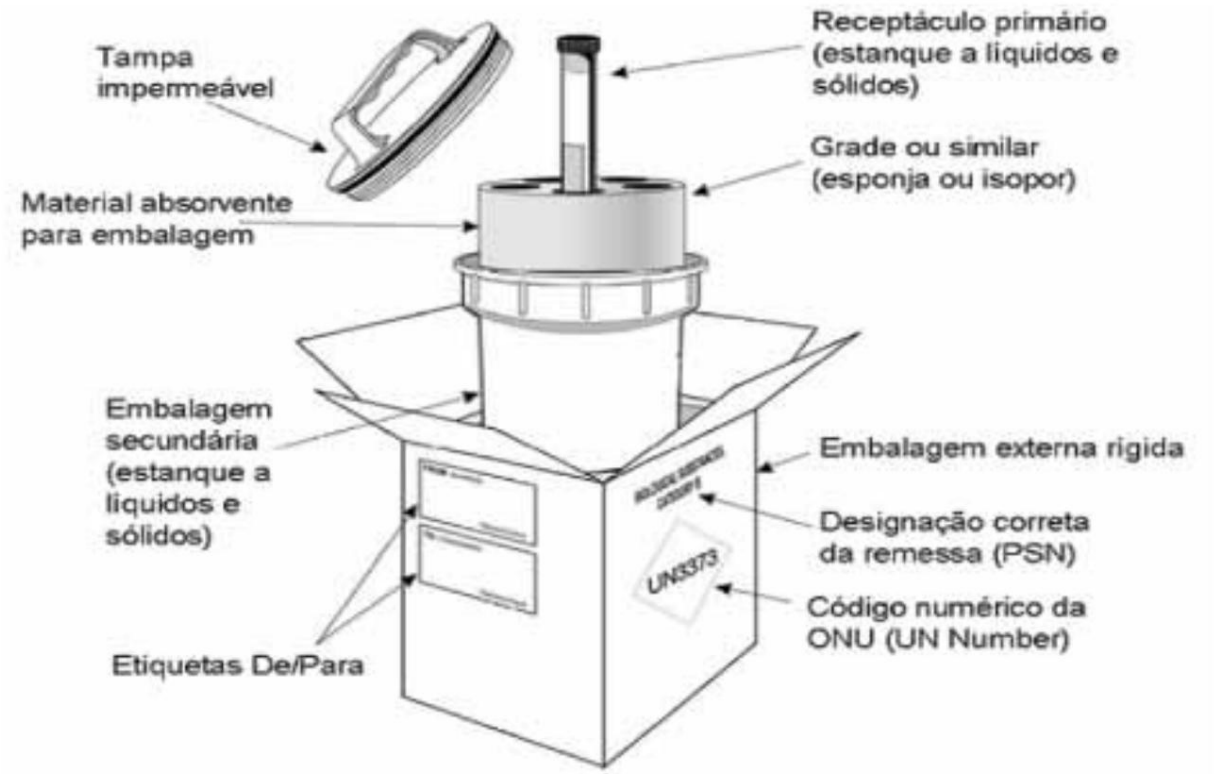
a) When using dry ice or liquid nitrogen to keep samples cold, there are some requirements for this type of transport set out in the transport regulations for dangerous goods. These materials will be discussed later. Ice or dry ice must be placed outside the secondary packaging, in the outer packaging or in the overpack. Interior supports must be provided to ensure that secondary packages remain in their original position after the dry ice or ice has dissipated. If ice is used, it must be ensured that there are no leaks in the outer packaging or the overpack. If solid carbon dioxide (dry ice) is used, the package must be designed and constructed to allow the carbon dioxide gas to escape, in order to prevent a build-up of pressure that could rupture the packages.

b) Primary packaging and secondary packaging must maintain their integrity for both the temperature of the refrigerant used and the resulting temperature and pressure if refrigeration is lost.

Biological substances assigned to UN 3373 are not subject to any other regulatory requirement for the transport of dangerous goods.

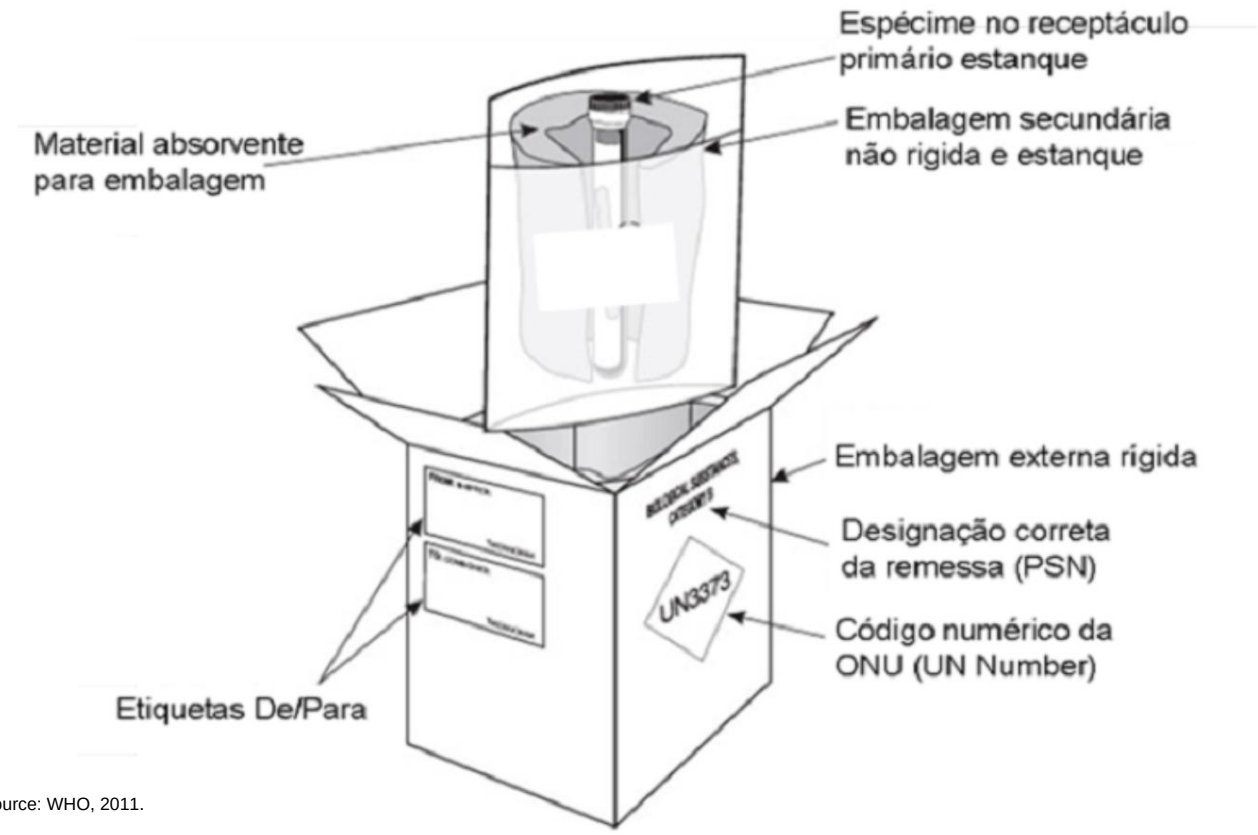
There is no requirement for certification or approval approval of category B packaging by transport regulatory agencies in Brazil. However, the package manufacturer must provide the shipper or person who prepares the package with clear packing and closing instructions to enable the package to be properly prepared for transport.

Figure 4 - Model I: transport packaging for category B.



Source: WHO, 2011.

Figure 5 - Model II: transport packaging for category B.



Source: WHO, 2011.

6.2.6. Markings and information on labeling

The packages must contain the markings and information required by current legislation, namely:

- Name and address of sender and recipient.
- Name and telephone number of the person responsible (who must be on standby 24 hours a day until the shipment arrives) for the transported contents, provided in a written document or inscribed on the outer packaging.
- Correct classification of the material to be transported: biological substance of category B.
- UN numerical code (UN 3373).
- If dry ice is used as a refrigerant, the Class 9 hazard label shown in Figure 3 must always be affixed to the outer packaging.

6.3. Documentation

These are fiscal documents of the cargo to be transported. RDC 20/2014 establishes that biological material must be transported with documentation that allows the traceability of the shipment/cargo transported. Thus, any tax document that assures the origin (sender) and destination (recipient) of the material being transported, together with the cargo risk identification labels, will facilitate the traceability and safety of the material.

6.3.1. Air transport (anac standards)

Category B biological substance transport requires the CT-e for domestic transport or the AWB for international transport.

6.3.2. Land transport (standards da ANTT)

Tax documents must contain some information, such as:

- Full address of recipient and name and telephone number of a person responsible for technical information on biological material.
- Information that identifies the vehicle or mode of transport to be used, the date of the transport and the name of the airport(s), the transfer station(s) and the place(s)) discharge (if applicable).
- Other information that the sender and recipient deem necessary.

6.4. Particularities of substance transport from category B

6.4.1. Air transport (ANAC standards)

The maximum quantity of Category B biological substances contained in a single permissible outer packaging is 4 l or 4 kg. This maximum quantity excludes the weight of ice, dry ice or liquid nitrogen used to refrigerate the hazardous article. These quantity limitations do not apply to the transport of body parts, organs or whole bodies.

6.4.2. Land transport (standards da ANTT)

Regarding land transport, there is no quantity limitation for the transport of biological substances of category B.

7. MINIMUM RISK HUMAN SPECIMEN

The requirements indicated below are defined by Anac.

Term adapted from English *exempt human specimen.* This category includes biological materials from individuals who have been subjected to professional judgment based on clinical history, symptoms and individual characteristics, as well as on local epidemiological conditions that ensure the minimum probability that the biological material contains pathogenic microorganisms, even if these materials do not have previously undergone laboratory tests for communicable disease markers.
This classification is defined in the WHO guidelines. In Australia, this material has been named category C or also *exempt human specimen.*

These biological materials are not considered infectious substances, that is, they are not dangerous goods for transport regulation purposes.

Examples of minimal risk biological samples, depending on the clinical assessment of the individual from whom the biological material was collected:

a) sample of blood, serum, plasma or urine to monitor levels of cholesterol, glucose, hormones, prostate specific antigen (PSA) etc.;

b) samples for functional monitoring tests of organs such as the heart, liver or kidneys of humans or animals with non-infectious diseases;

c) samples for drug monitoring tests;

d) samples for pregnancy tests;

e) biopsies to detect cancer;

f) tests to detect antibodies in humans or animals, provided that there is no suspicion of infection (assessment of vaccine-induced immunity, diagnosis of autoimmune diseases, etc.);

g) samples collected from donors of blood, tissues, cells and organs after clinical and epidemiological screening, by health professionals, in specialized services/banks;

h) samples for drug or alcohol testing without suspected infection.

It is worth remembering that patient samples can be considered as minimal risk human specimens, provided they have documented professional judgment.

To determine whether a patient sample has a minimal probability of the presence of pathogens, professional judgment is required. This judgment is based on known clinical history, signs and symptoms, and local epidemiological conditions. Professional judgment must be evidenced by a document that accompanies the transport of biological samples and that contains, at least, some information, according to Anac standards.

Information for professional judgment for classifying a biological material as a minimal risk human specimen

- Professional's full name, CPF and/or professional council registration number.
- Laboratory service, health service or professional link company, with CNPJ, full address and contact telephone numbers.
- Affirmation that this is the transport of material classified as a human specimen of minimum risk and that it does not fit into another class of dangerous goods.
- Description of the mechanisms used for classification as a minimal risk human specimen (non-reactive/ negative tests, aptitude for clinical screening, knowledge of clinical history, etc.).
- Description of the quantity of samples to be transported.
- Declaration of the type of packaging.
- Declaration with the respective amount of refrigerant material (ice, dry ice, gelox, gel ice, liquid nitrogen, etc.).
- Data.
- Signature of the responsible professional.

These requirements for professional judgment were established by Anac and seem to be useful for any type of transport.

When it is not possible to evaluate the biological sample by a duly trained professional or the sample is transported for the purpose of diagnosing infectious diseases, it must be classified as a category B biological substance.

7.1. Packaging, labeling and labeling

The packaging for transport, known as triple packaging or triple packaging, must be composed of three components: a) watertight primary container; b) watertight secondary packaging; and c) rigid (tertiary) outer packaging of adequate strength for its capacity, mass and intended use.

The primary packaging must be equipped with a device that guarantees a leak-proof seal and must be impermeable to liquid samples; in the case of solid or semi-solid samples, it must consist of a resistant container equipped with a closing mechanism that prevents the material from overflowing. For example, sample tubes (glass or plastic) are considered primary packaging or containers.

The secondary packaging, impermeable and leak-proof, must be made of resistant material, in order to contain the primary packaging. Plastic bags are widely used as secondary packaging.

Rigid tertiary packaging must be resistant, of adequate size for the biological material transported and equipped with a closing device, noting that washable and disinfectant-resistant materials can be reused. For air transport, the minimum dimensions of this package are 100 mm x 100 mm. Plastic boxes (PVC), cardboard, metal, drums or other rigid materials are examples of tertiary packaging that can be used.

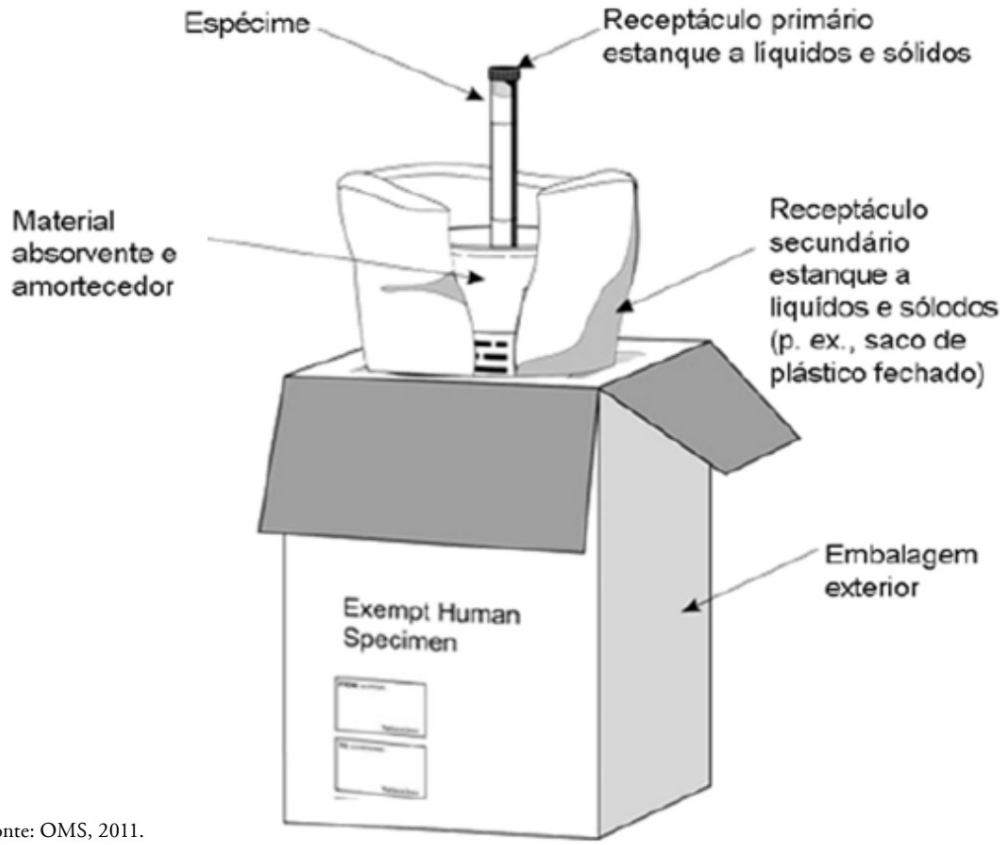
Expanded polystyrene (Styrofoam), plastic bags and other materials without proper rigidity, strength and impermeability are not permitted as outer packaging for transporting clinical specimens.

For biological samples transported in fragile inner packaging, susceptible to breakage (eg glass tubes), hole or crack, it is necessary to observe the following aspects:

I - the arrangement of the primary packaging(s), in order to avoid collisions with each other and/or with the packaging that surrounds them, in order to maintain the integrity of the transported material. The container or tube for transporting clinical samples of fragile material must be packed in secondary packaging, organized in such a way as to avoid spillage of biological material and impact on each other, if two or more tubes (other containers) are transported together. The service must develop a device (shelves, partitions or similar) to organize the pipes. When using break-resistant primary packaging, such as plastic tubes with a secure and leak-proof closure device, it is possible to pack several tubes together, without the need for a separating device between them.

II - for liquid samples, absorbent material must be used as part of the packaging system, in order to absorb the entire contents of the primary packaging(s) in the event of material leakage. The absorbent material can be sponge, absorbent paper, cotton, fabrics and others.

FIGURA 6 – MODELO DE EMBALAGEM PARA MATERIAL BIOLÓGICO DE RISCO MÍNIMO.



Fonte: OMS, 2011.

7.2. LIMITAÇÃO DE QUANTIDADE

Não há limitação de quantidade aplicável ao espécime humano de risco mínimo.

7.3. ETIQUETAGEM

Não há etiqueta de risco aplicável a este tipo de material biológico, ou seja, não se deve usar o símbolo de risco biológico na embalagem externa de transporte de material biológico de risco mínimo.

7.4. MARCAÇÃO

A marca presente na embalagem externa é a frase: **Espécime humano de risco mínimo**, em português, ou *Exempt human specimen,* em inglês, conforme apropriado.

Não há código de número da ONU (UN) para espécime humano de risco mínimo.

NÃO HÁ ETIQUETA DE RISCO APLICÁVEL AO ESPÉCIME HUMANO DE RISCO MÍNIMO

7.5. Documentation

The carrier of the minimal risk human specimen needs to carry fiscal documents that allow the traceability of the shipment/cargo transported, along with the document of professional judgment.

7.5.1. for air transport

In addition to the professional judgment document, CT-e must be provided for domestic transport or AWB for international transport.

8. EXEMPT BIOLOGICAL MATERIAL

The requirements for the transport of exempt biological material discussed below are defined by Anac and adopted by Anvisa's RDC 20/2014.

Human biological materials not included in the previous classifications, which are known to be free from infectious agents or have undergone neutralization/inactivation/ sterilization processes, whether dry biological materials collected in specific devices, such as absorbent paper, or blood and components produced for transfusion , cells, tissues and organs for transplantation will be classified for transport purposes as exempt biological materials.

The following biological samples do not present infectious risks during the transport process, being considered exempt biological materials:

a) samples that do not contain infectious substances or agents;

b) samples containing microorganisms that are not pathogenic for humans or animals;

c) samples in which all pathogens present are neutralized/sterilized or inactivated in such a way that they do not pose a health risk;

d) environmental samples (including food and water samples) that do not pose a significant risk of infection;

e) dried blood spots, collected by applying a drop of blood to an absorbent material or similar mechanism;

f) biological samples intended for fecal occult blood screening tests;

g) bag of whole blood or blood components that have been released for transfusion purposes;

h) any cells, tissues or organs released for use in transplants or grafts.

8.1. Packaging, labeling and labeling

RDC 20/2014 determines that exempt biological materials are transported in packaging as defined for minimal risk biological materials or another packaging mechanism that guarantees the conservation of the biological properties of the material.

There is no quantity limitation applicable to exempt biological material.

THERE IS NO RISK LABEL APPLICABLE TO THE MATERIAL BIOLOGICAL EXEMPT

There is also no label or marking applicable to exempt biological material, which cannot use the biohazard symbol.

8.2. Documentation

The transport of exempt biological material requires the CT-e for domestic air transport or the AWB for international air transport, as well as the professional judgment document.

Some of these materials (eg, biological products for transfusion, graft and transplant purposes) have specific transport regulations.

Anvisa recommendations!

9. BIOSAFETY

The personnel involved in the transport process must have collective and individual protection equipment, according to the risk involved in the activities of handling the biological material. In normal situations, during the transport process, material handling takes place during packaging in the sending laboratory and on receipt of samples at the receiving service. Personnel responsible for these activities are at risk of direct exposure to human biological material and must be vaccinated in accordance with worker health standards.

Regardless of the risk classification of the biological material transported, when any individual responsible for packaging, transporting or opening the packaging of biological material perceives that it is damaged or leaking, he must:

I - avoid handling the packaging or reduce it to a minimum;

II - inspect adjacent packages to verify if they have been contaminated and separate those that may have been contaminated;

III - inform the local authorities (police, fire department, etc.) about the fact;

III - inform the appropriate public health authorities (sanitary, epidemiological surveillance, etc.) that have danger of contamination; and

IV - notify the sender and recipient.

Vehicles that have been contaminated by biological materials must be washed with running water and treated with appropriate disinfectants, in a suitable place.

RDC 20/2014 does not apply to the transport of biological waste generated in health services. To this end, attention must be paid to the requirements contained in RDC 306/2004, which approves the Technical Regulation for the Management of Waste from Health Services.

Immediate procedures after extravasation: do not touch. Contact qualified personnel.

Anvisa recommendations!

10. DOCUMENTATION

The transport process is part of the laboratory production cycle and must be part of the quality assurance policy developed by the laboratory.

All critical transportation activities must be recorded, either physically or electronically. The standardization of transport process procedures aims to prevent, detect, identify and correct errors or variations.

Transport operations must be recorded and standardized through up-to-date written instructions.
Written and standardized instructions must be available to all personnel involved in the transportation process and must be reviewed annually and/or whenever there are changes to procedures.

All laboratory activities must be documented through work instructions (IT) or standard operating procedure (SOP) approved and available to all personnel who will perform the defined activities.
Electronic media can be used for storage and even in routine transport, as long as they are complete, updated and available to professionals in a timely manner.

During the biological material transit stage, the carrier must carry a document that allows the traceability of the shipment/cargo transported.
Depending on the mode of transport used and the risk classification, specific documents must be prepared.

The clinical laboratory must define the criteria for the management of documents related to transport, establishing the period and form of archiving. Records deemed critical by the laboratory must be kept for at least five years.

11. OVER-PACKING

It is a wrapper used by a single shipper/sender to house one or more packages/boxes, forming a unit, for convenience of handling and/or organization during transport.

When more than one complete package (a system made up of primary, secondary and tertiary packages) is placed in a protective outer packaging (for example, boxes, plastic materials or crates), we can identify an overpack.

According to Anac and ANTT standards, the following information must be placed on the outside of a non-transparent overpack:

- the appropriate name for transport (eg, Category B biological substance; minimal risk human specimen, etc.);
- the UN number (UN 3373, UN 2814), depending on the risk classification;
- the labels/tags corresponding to each dangerous product it contains (senders, recipients, warnings, etc.).

Each packaging/box system with biological material contained in the overpack must comply with all applicable regulatory provisions. The function assigned to each packaging system must not be jeopardized by overpacking, that is, individual packages must be packed completely and in accordance with the risk of the transported biological material.

When packages containing category A dangerous goods are placed in an overpack, the biohazard label on each package must be clearly visible. If it is not possible to see the boxes inside the overpack, the biohazard label must be affixed to the outside of the overpack, as well as the term “about packaging”, in Portuguese, or *overpack,* in English.

12. REFRIGERANT MATERIALS

The requirements indicated below are defined by Anac and ANTT.

12.1. Ice, dry ice, liquid nitrogen

When it is necessary to maintain the refrigerated or frozen state of the biological material during transport, it will be necessary to use certain refrigerants such as ice, dry ice, liquid nitrogen or cryogenic liquids.

Ice, dry ice or other refrigerant material should be placed around the secondary packaging(s) or, alternatively, in an overpack, as the shipper (laboratory) determines for the best conservation of the material.

Inner supports must be placed to ensure that secondary packaging or other packaged materials remain in their original position after the dry ice sublimates or the ice melts.

If ice is used, the outer packaging or overpack must be leak-proof; if dry ice is used, solid carbon dioxide (dry ice) must be able to escape through the cracks in the outer packaging.

The packaging system must maintain its integrity at the temperature of the refrigerant used. The materials that form the packaging system (plastic, cardboard, metals and others) must be able to withstand the related temperatures.

12.1.1. Dry ice

Dry ice is the most commonly used hazardous item as a refrigerant.

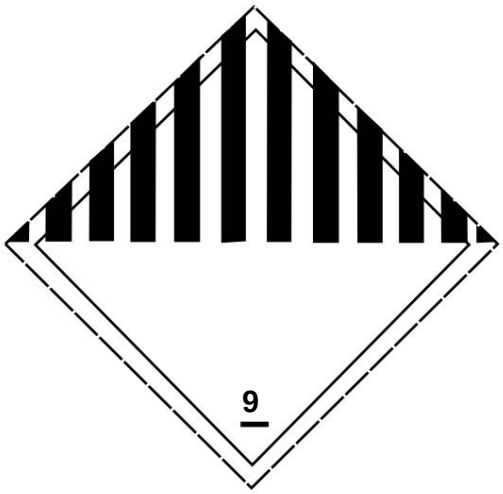
Dry ice is identified with the **UN number 1845** and the appropriate name for transport: “solid carbon dioxide” or “dry ice”, in Portuguese, or *carbon dioxide, solid* or *dry ice,* in English.

It is not considered necessary to carry out specific packaging tests for the transport of dry ice, drawing attention to the compatibility of the ice with the different packaging materials and the closing requirements. Packages must be designed and constructed to facilitate the release of carbon dioxide gas, in order to avoid a build-up of pressure that could rupture them.

Figure 7 - Schematic drawing for substances miscellaneous hazards.

The label must be in the shape of a diamond with minimum dimensions of 100 mm x 100 mm. In addition

In addition, the liquid mass of dry ice transported must be informed on the external packaging.



Source: WHO, 2011.

In relation to air transport, the airline must be notified of the use of these types of refrigerants to ensure that ventilation safety procedures are followed.

Air transport of dry ice requires the following documents:

a) CT-e for domestic transport or AWB for international transport;

b) Notoc (Notification to Commander).

For both land and air transport, cargo containing solid carbon dioxide (dry ice) is exempt from shipping documentation requirements if the package contains the expression “SOLID CARBON DIOXIDE” or “DRY ICE” and an indication that it is biological material under refrigeration for diagnostic or treatment purposes (eg frozen biological samples).

12.1.1.1. Quantity limitation

In land transport, there is no limitation on the amount of dry ice as refrigerant.

In air transport, the maximum allowed quantity of dry ice contained in a single package is 200 kg, both for passenger and freighter aircraft.

Anvisa recommendations!

13. SANITARY LICENSING

The transport of biological samples is part of the activities performed by the clinical laboratory and, with regard to pre-analytical procedures, it is a step considered of paramount importance for the quality assurance of the tests performed.

The clinical laboratory and the laboratory collection point must have an updated health permit/license issued by the competent health surveillance agency (state or municipal Sanitary Surveillance), after evaluating the structures and processes involved in the laboratory service, according to RDC 302/2005 of the Anvisa. Among other items, the transport processes (packaging, transit and receipt) and the structural conditions of the vehicles that will carry out the transit of biological material must be evaluated.

The health standards used as a standard for the evaluation process of the transport of clinical samples are RDC 302/2005, which provides for the Technical Regulation for the Operation of Clinical Laboratories, and RDC 20/2014. In addition to these, other state and municipal health regulations, complementary to the aforementioned federal health regulations, must be followed, referring to the transport of biological samples for the purpose of clinical diagnosis.

It is up to the local Sanitary Surveillance (Visa), according to loco-regional assessment, to determine specific inspection mechanisms for sanitary control of the transport process and to guide this process. It is worth remembering that many Visas also call health licensing as a health permit or operating license.

When the laboratory carries out the activity of transporting clinical samples as part of its attributions and with its own vehicles, this is inherent to the assessment of Visa and must be part of the list of activities of the clinical laboratory. In this way, the health permit of the clinical laboratory would already include the licensing for the transport activity. the laboratory

clinician should consult local Visa regarding settlement processes.

When the clinical laboratory does not have adequate infrastructure for the safe and quality transport of biological samples and hires services from third parties, the outsourced transport service provider must be legally constituted and licensed in accordance with the requirements established by health standards. Visa will evaluate the infrastructure available for transport, the number and qualification of employees, according to the activities performed, as well as technical supervision.
When hiring a specialized outsourced company to perform an activity of interest to health, it needs to be officially recognized by regulatory bodies, through health licensing, as a transport company suitable for the provision of the services it intends to offer, configuring a typical regulatory practice against information asymmetries and negative externalities.
Many transport companies are specialized in the transit of medicines, vaccines and other products and have experience in transporting material under refrigeration. These companies have sanitary licensing and authorization from Anvisa for the transport of pharmaceutical products and can include in their activities the transport of clinical samples for diagnosis, as long as they meet the specifications for this type of cargo and undergo local Visa assessment.

exceptions

RDC 20/2014 defines that government companies/services that transport biological material, under a contract with the Ministry of Health or public management bodies or entities, are not subject to sanitary licensing. We can list some government institutions, such as public security agencies (Federal Police, Federal Highway Police, Civil Police, Military Police and Fire Department), mobile emergency services (Samu), civil defense agencies, Armed Forces (Army , Aeronautics, Navy), public postal services, among others of a similar nature. In this case, there is a need to formalize the provision of services through written instruments between the competent health authorities (Ministry of Health, state and municipal health departments or related health bodies) responsible for health management at different levels of government and government institutions public service providers.

Another exception to health licensing is when the laboratory service uses, in its transport process, the services of a passenger and cargo transport company (bus, airline and others). these companies transport of passengers and their loads are regulated and inspected by ANTT (land transport), Anac (air transport) and Antaq (water transport) through specific rules applied to the transport of biological material. Thus, they are not subject to licensing by the health surveillance.

In either of the two exceptional situations, RDC 20/2014 and other related standards establish that the health surveillance must evaluate, when it deems necessary, the technical-sanitary conditions of transport, since these bodies must meet the technical, operational and legal aspects. inherent to their activities.

In addition, RDC 20/2014 defines that in the event that the sending laboratory uses, in its transport process, the services of a road, rail or waterway passenger and cargo transport company and of air operators that are not subject to licensing The laboratory will be responsible for verifying the technical conditions in which the material will be transported and monitoring the delivery and arrival of the material to its final destination. This responsibility must be clearly established in formal documents.

The sanitary license is a document that guarantees that the establishment or company has sanitary conditions to carry out certain activities related to public health.
There is no provision for this document or copy to be physically in the vehicle transporting biological material during transit. It is established that the carrier must carry documents that guarantee the identification and traceability of the transported cargo.
However, it should be noted that the licensing, both for the laboratory and for the outsourced carrier, must be accessible to the citizen whenever requested, as a means of proving the Visa assessment regarding the activity.

RDC 20/2014 does not define local Health Surveillance workflows, due to the local and regional specificities involved in terms of the transport of biological samples for clinical diagnosis in the national territory.
Each municipal and state health surveillance authority can establish requirements and work designs, according to their realities. The national guideline is that all transport/ transit of biological material is carried out by a service or transport company duly licensed by a Visa agency or under its formal responsibility.

In this way, the Visa responsible for the place where the sender is based must assess how the transport of biological samples takes place, adding to the laboratory assessment the transport infrastructure (if transport is carried out

own) or requiring the contracted transport company to have a sanitary license.

The Visa responsible for the place where the recipient is headquartered must assess the conditions for receiving the biological material and require the licensing of the service or company that carries out the transport. It is noteworthy that each situation must be evaluated with the Visas involved, for the purpose of standardizing these flows and processes.

14. CARRIERS AND VEHICLES

The carrier may be a person or institution that transports human biological material from a sender to a specified recipient.

The transport vehicle must have adequate hygiene and cleaning conditions, as well as having a mechanism that ensures the integrity of the tertiary packaging and the transported biological material. Devices for securing packages to vehicles must be used to ensure that they remain secure during transit.

The land transport vehicle must always be in perfect conditions of use and meet the legal requirements of the National Traffic Council (Contran) and ANTT.
In addition, it must have received preventive maintenance and be suitable for the material transported.

When the service uses its own vehicles in the transport process, it can be said that it transports its own cargo. In this case, the activities of transporting clinical samples are part of those licensed by the health surveillance to the aforementioned laboratory.

When the transport infrastructure (vehicles, personnel, logistics, etc.) is carried out by third parties, through a formal outsourcing document, it must be carried out by a legal entity duly regularized by the health surveillance.

Passenger and cargo buses can transport certain types of biological materials in their cargo compartments, through a formal outsourcing document. Permissions and prohibitions for transporting specific biological materials in passenger vehicles (buses) must be verified with ANTT.

This prerogative also applies to passenger and cargo air operators (civil aviation companies). These carriers are regulated and supervised by the agencies transport regulators, through specific rules for the transport of biological materials.

Vehicles or urban trains for public land transport (eg circular buses, subways, minibuses, trams, etc.) are not considered cargo carriers and therefore should not be used to transport biological material from health services. An exception to this case occurs when the individual transports biological material considered for his/her own use, in hand/accompanied luggage in a quantity never exceeding 1 kg or 1 l per passenger. Thus, except for the permission prescribed above, biological materials cannot be transported in urban passenger transport vehicles.

Motorcycle: according to the Brazilian National Traffic Code, the motorcycle can be considered a self-propelled cargo vehicle. In this way, it can constitute a transport vehicle for clinical samples belonging to the clinical laboratory or be part of an outsourced company licensed for the transport of biological material. The main laws that govern transport by motorcycles and
scooters are:

- Law 12,009, of July 29, 2009 – regulates the exercise of the motorcycle courier.
- Law 12,436, of July 6, 2011 – prohibits practices that encourage speeding up by professional motorcyclists.
- Contran Resolution 356, of August 2, 2010 – establishes minimum safety requirements for motor-freighters.
- Contran Resolution 350, of June 14, 2010 – institutes a mandatory specialized course for motorcycle couriers.

Attention: companies that use motorcycles/motor scooters should contact the Traffic Department (Detran) of their localities to regularize this type of cargo transport vehicle.

Post (postal): Category A dangerous goods are generally prohibited from being transported by post. However, biological samples intended for clinical diagnosis falling under Category B – UN 3373, packaged in accordance with Packaging Instruction 650, as well as solid carbon dioxide (dry ice), when used as a refrigerant in UN 3373 packaging, may be transported by post, both by air and by land. It should be noted that biological materials classified as minimal risk human specimens and exempt biological materials can also be transported by post (Law 6,538, of June 22, 1978).

Taxi: Passenger road taxi cannot be considered a commercial cargo vehicle. The transport of samples by taxi services could be carried out as cargo accompanied by a properly trained laboratory professional (own transport). Many municipalities and states have specific legislation to discipline taxi services; thus, one should consult related bodies regarding permissions and prohibitions for the transport of biological material.

Anvisa recommendations!

15. TRAINING

Training and awareness is important for all personnel involved in transporting biological samples.
Only through adequate guidance and training can shippers/senders guarantee the correct classification of the sample that will be sent and the correct selection of materials that make up the packaging system, as well as prepare and package the biological material in order to keep it safe during transit to your final destination.

As it is a complex process, with several actors involved, the responsibilities for the preparation, execution and evaluation of training must be defined in contracts, agreements, terms of responsibility or other similar documents. Each party involved may be responsible for training its personnel or for training other parties. The important thing is that responsibilities are formally defined by the parties.

The **sender,** in general, should have knowledge of:

- the technical and legal requirements established in the applicable legislation;
- the characteristics of the material being packaged (conservation and biological risk);
- the stages of the packaging process;
- the types of inputs used (refrigerant material, organization devices, packaging, absorbent, cushioning materials, etc.);
- the laboratory's standardized operating procedures;
- information on labels, tags and markings used;
- documents necessary for dispatch;
- the logistics to be used for transit;
- routine biosafety conducts and in cases of accidents with biological material;
- other skills that the laboratory considers important for the training of the sender.

Among the sender's responsibilities, the classification of the transported material stands out. The latter is responsible, both administratively and criminally, for possible errors. One of the biggest problems observed in inspections and incident notifications on Brazilian aircraft is errors in the classification and packaging of biological material. For example, the sender/shipper informs that it is a minimal risk human material and is actually a category B biological substance (UN 3373), or states that adequate packaging has taken place in triple packaging, when what actually happened is that the tubes fragile were packed together, bumping and breaking during transit.

The **carrier** must be trained to understand:

- the technical and legal requirements established in the applicable legislation;
- the general characteristics of the material being transported (conservation and biological risk);
- the standard operating procedures for the phases of the process it performs (eg loading the cargo onto the vehicle, procedure in case of delays, accidents or other non-compliances, unloading and delivery of the cargo, etc.);
- the cargo documents;
- the correct use of the available infrastructure to ensure the safe transit of transported material;
- the logistics to be used for transit;
- biosafety conducts in cases of accidents with biological material;

• other skills that the carrier considers important for their training.

Biological material can only be transported after acceptance by the carrier. This acceptance consists of verifying that all visible requirements (packaging, markings, labeling, documentation, etc.) comply with technical standards.

At a minimum, the recipient must know :

- the technical and legal requirements established in the applicable legislation;
- the general characteristics of the material being received (conservation and biological risk);
- the necessary conditions for the conservation and stability of the biological material received;
- the standard operating procedures for the phases of the process it performs (eg, receiving the cargo, assessing the quality of the material that has been transported, etc.);
- the cargo documents;
- biosafety conducts for routine and in cases of accidents with biological material;
- other skills that the laboratory considers important for the training of the recipient.

The laboratory must develop and implement a training program that determines the issues to be addressed to the professionals involved in each stage of the transport process, as well as the frequency of training.

Carriers must be trained in the proper procedures to recognize and take due care of packaging containing biological materials and to deal with spills and accident situations with extravasation of biological material, such as cases of vehicle collision, spillage of biological material , vehicle and soil contamination, etc. Carrier training should focus on safety awareness, noting the nature of the hazards involved, how to recognize such hazards, methods to mitigate them and the actions that should be taken. It should also include awareness of the importance of ensuring transit within the established time and what to do in situations of delays, having as a premise the essential function that that material represents for an individual who depends on its proper conservation for the quality of his clinical diagnosis.

The training of air transport agents, in addition to aspects related to the general philosophy, limitations, labeling and marking of specific requirements for passengers and crew and emergency procedures, must include elements of awareness related to in-flight safety.

UN 3373 samples packaged as PI 650, per ANTT and Contran standards, are exempt from complying with all other hazardous goods regulations and therefore do not need special vehicles, dangerous goods signage, or specific driver training to transport dangerous goods (dangerous goods handling course or operational handling of dangerous goods – Mopp). It is worth remembering that the Mopp is essential for training drivers who transport Category A infectious materials by land. In any case, this exemption applied to the transport of biological materials of category B, specimens of minimum risk and exempt materials does not exclude the need for the driver to receive training directed to the activities that he will develop in the context of transport, containing basic knowledge about the process of conservation of biological material, biosafety instructions and guidelines in case of accidents, among other applicable topics.

If the driver has taken the Mopp course, this professional is able to competently and safely carry out the transport of biological material, especially in relation to conduct in the event of accidents or other damage. However, it is important to complement their training with knowledge about the characteristics of clinical samples and their importance in the context of public health.

Regarding land transport, ANTT Resolution 420/04 is based on previous editions of the UN Model Regulation (Orange Book), not including the updated classifications – category A, category B and others for biological materials. In this way, the current version of the aforementioned ANTT resolution does not present exemptions for category B, but is in the process of review and update and should soon observe the same classification.

In relation to air transport, the airline must have authorization from Anac for the transport of infectious substances (dangerous articles) and its employees must be trained according to the responsibility of their functions.

In general, training records must include the names of the trainees, the role performed, the topics studied, a description of the teaching methodology used, the identification of the instructors, the duration and date of the training, as well as the declaration that the training was successfully completed and evaluated.

16. CONSERVATION OF

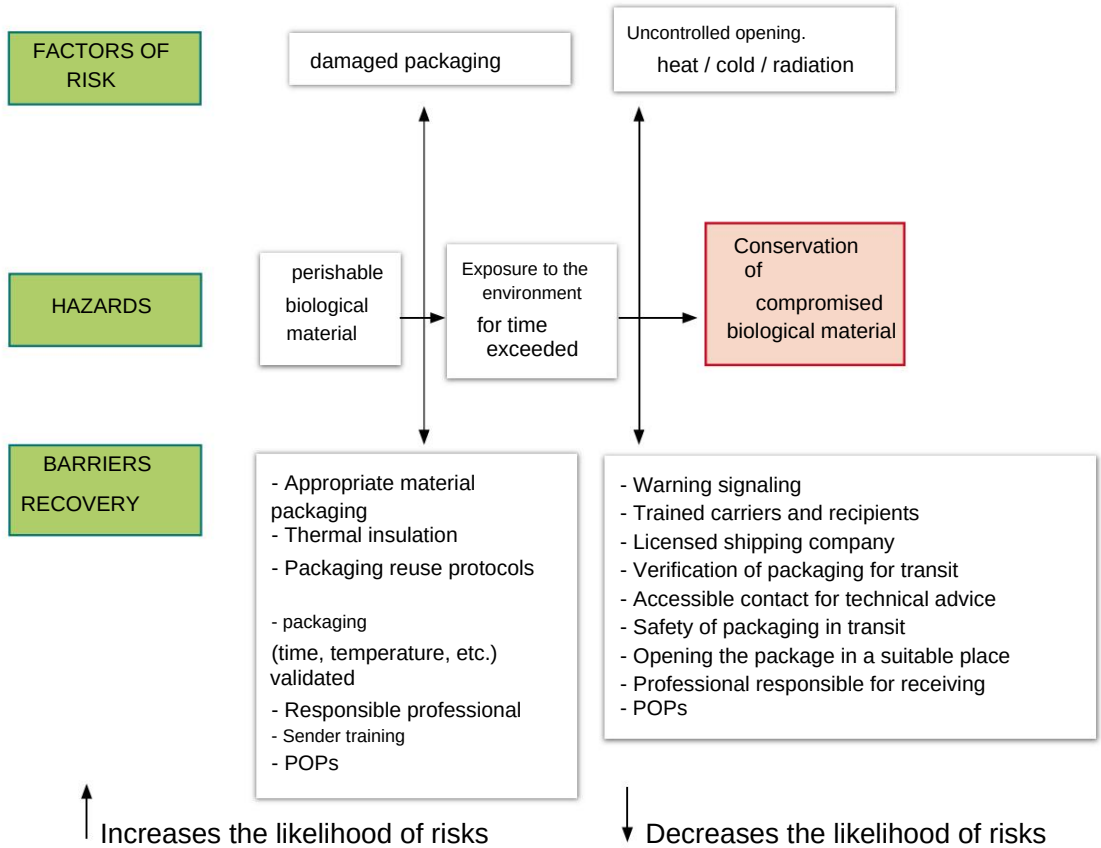
BIOLOGICAL CHARACTERISTICS

Regardless of the set of packages that will be used for the transport of clinical samples, these must be designed in a way that allows the maintenance of the biological properties, according to the characteristics of each transported material.

In Figure 8 it is possible to demonstrate the configuration defined in RDC 20/2014 to establish the control items in the transport of biological material, focusing on the stability and conservation of its characteristics.

Figure 8 - Risk management of conservation of biological material during transport.

Source: Anvisa, 2014.



These materials need to be transported in order to maintain their integrity to their final destination. A major regulatory concern is ensuring adequate temperature throughout the entire path, as well as the physical integrity of this material.

To this end, transport validation is essential and includes the stages of packaging, transit and receipt of biological material. The sample packaging standard, as well as the definition of the appropriate temperature range for the transport of biological samples to their final destination, is the responsibility of the laboratory that stores the material and must take into account the instructions of the manufacturer of the kits/reagents to which these samples will be submitted and the literature/methodology applicable to the examinations. This information will be taken into account during the validation stage and must be included in the operational procedures used in the laboratory.

Anvisa recommendations!

16.1. validation of transport process

Regarding the conservation of biological material, the set of packages must be validated taking into account the quantity and characteristics of the biological material transported, as well as the type and quantity of refrigerant material in relation to the transport time, including possible delays and ambient temperature conditions along the route.

The laboratory must validate its transport process considering the following criteria, among others applicable:

1) Packing of samples in the packaging system:

- Use of standardized packaging (primary, secondary and tertiary) used in routine.
- Assembly of the packaging system, based on each type of biological material to be transported.
- Time required for the stabilization of the internal temperature of the packages that will compose the system.

2) Acceptable temperature range to ensure the stability of the analytes, according to the instructions of the manufacturer of the kits/reagents to which these samples will be submitted and the literature/methodology applicable to the examinations.

3) Quantity of biological material, refrigerant material and absorbent material, according to each box size.

4) Transport period, considering a safety margin in case of unforeseen events during the transit of biological material and extremes of ambient temperature.

The validation process must be described through validation protocols and final validation reports, and must be reviewed by the laboratory, when necessary, thus ensuring the maintenance of the established process.

When temperature control is required during the transport of biological material, the laboratory must evaluate control options and determine which is most suitable for its process.

Some options for temperature control devices can be mentioned:

- continuous temperature monitors (example: *data loggers);*
- thermometers that record the maximum and minimum temperature coupled to the packaging system during the entire transport;
- determination of the temperature at the origin/output and at the destination/receipt;
- any other temperature measuring equipment can be considered in this process, as long as it is properly calibrated and with a certification record approved by the clinical laboratory.

Note: During validation, the standardization of conducts to be adopted in cases of receipt of material with temperature outside the established range must be evaluated. The laboratory must analyze the margins of acceptable temperature deviations that do not compromise the quality of the analytes and, consequently, the reliability of the results. With this definition, one must take the action of accepting/processing or refusing/discarding the biological material.

16.2. Characteristics of biological samples for diagnostic purposes

Samples sent to any diagnostic laboratory must have proper identification and labels must use material that is resistant to handling, ie permanent water resistant inks, tape with glue or labels with appropriate adhesive.

Transport is a complex activity that must observe requirements related to safety and maintenance of the characteristics of the transported product/sample. When talking about clinical samples for diagnosis, there are a variety of types of samples and each one requires specific care. The laboratory is responsible for defining the technical criteria, according to the characteristics of the biological materials and technologies it uses, and must maintain written records and protocols.

16.2.1. Body fluids

Whole blood samples need to be processed as quickly as possible from the perspective of separating cells from plasma and serum. It is recommended that separation be performed within two hours of collection of whole blood. Thus, the transport that takes place from the collection area to the sample processing area must be as fast as possible.

Not all biological properties of a sample deteriorate as quickly. Some analytes require certain temperatures for their conservation. In general, there are three basic temperature ranges, depending on the material:

- Ambient temperature: 18°C to 25°C.
- Cooling temperature: 2°C to 8°C.
- Freezing temperature: below -18 ° C.

Samples intended for labile factor examinations must be transported as quickly as possible, within the appropriate temperature range to ensure the quality of the analysis.

The evaluation of the sample upon receipt by the recipient is of paramount importance for the quality of the test. The sample volume, the degree of hemolysis and signs of coagulation, alterations that may occur during the transport process, must be analyzed. This assessment depends on the type of biological material and it is up to the recipient laboratory to establish acceptance requirements.

16.3. Guidelines

If the clinical laboratory and the collection point choose to outsource the transport of biological material, there must be a formal contract observing the criteria established in RDCs 302/05 and 20/14. This link must be available at participating establishments, that is, there must be a copy of the contract, term of responsibility, agreement or other types of formal documents with the carrier, the clinical laboratory and the collection point. Responsibility for transport is shared by all involved, but it is the clinical laboratory and the sending collection point that will define the written instructions on transport, determining deadlines, temperature conditions and technical standards to ensure the integrity and stability of the material. . The logistics operator must know and apply these instructions, being responsible for all activities inherent to its phase of the process, duly defined in a formal outsourcing instrument.

Anvisa recommendations!

ANNEX I - Transport Validation Protocol Model

Field 1: **Institution logo**
The placement of the laboratory logo is recommended.

Field 2: **Title of the document** This
field must contain the name given to the document, such as: “Protocol for Validation of Transport of Biological Samples under Refrigeration”.

Field 3: **Version**
This field must contain the version number of the document.

Field 4: **Document number** This field
must contain the number or alphanumeric code to be defined by the institution.

Field 5: **Prepared by**

This field must contain the name and position of the person or persons who prepared the document. The date on which the preparation of the document was completed, with its respective approval, must also be included.

Name: _____ Name: _____

Position: _____ Position: _____

Data: _____ Data: _____

Field 6: **Approved by**

This field must contain the name and position of the person or persons who approved the document. The date on which the approval of the document was completed must also be included.

Name: _____ Name: _____

Position: _____ Position: _____

Data: _____ Data: _____

Header

institution logo	Institution Name				
	Title: Transport Validation Protocol for ...				
	Number:	Revision:	Approval date:	Effective date:	1/2 sheet

Field 7:

1. INTRODUCTION

In this field, the document in question must be presented, expressing its relevance and the benefits arising from carrying out this activity. The motivations and circumstances for carrying out the transport validation must also be included in this field.

Field 8:

2 – OBJECTIVES

This field must include the general objective and the specific objectives, described in the infinitive and clearly.

Field 9:

3 - SCOPE AND RESPONSIBILITIES

In this field, detail the areas and people of the institution that will be involved in carrying out the validation study, as well as in the routine transport process. The responsibilities to be exercised during the validation study must be properly defined and described in this field.

Field 10:

4 - REFERENCES

In this field there must be a description of all documents used for the preparation of this protocol, as well as the documents to which this protocol refers.

institution logo	Institution Name				
	Title: Transport Validation Protocol for ...				
	Number:	Revision:	Approval date:	Effective date:	Sheet 2/3

Field 11:

5 - PROCEDURE

This field was subdivided into sub-items, leaving the laboratory to decide the way that best portrays its process.

5.1 - Transport processes

In this field, the detailed procedure of the previously established sample transport process must be described or the document where such information is found must be referenced. It is important that the materials to be used (boxes, refrigerant material, etc.) are defined, as well as the packaging configurations, with the respective quantities of bags and refrigerant material to be packed in each box.

Note: It must be informed which type of validation will be conducted, ie, concurrent validation or prospective validation. In the case of concurrent validation, the transport POP already exists and is used in the routine. This SOP and its respective version can be mentioned in this Protocol, not being necessary to transcribe the SOP in this field. In the case of prospective validation, a transport procedure to be studied must be defined.

5.2 - Storage and transport conditions of blood and components

This field must contain the temperature ranges in which the materials must be stored.

5.3 - Materials

All materials necessary for the previously defined sample transport process must be described in this field. Its identification and specifications, as well as the identification of material suppliers, must be included in this document.

5.4 - Validation process

Describe in detail the procedures to be adopted to carry out the validation, as well as the parameters to be monitored (temperature and time) and the acceptance criteria for a successful validation. At least three consecutive runs should be planned, establishing the maximum and minimum number of biological material to be transported in a box, the amount of refrigerant material to be used, the distribution of temperature thermometers inside the containers of transport (if applicable) and the transport time to be validated. Figures illustrating the distribution of packaging elements are useful for a better understanding of the task at hand.

Note: If temperature thermometers are used, they must be properly calibrated. Copies of the certificates of the instruments used in the calibration must be provided by the company that carried out the calibration of such registers and must appear as annexes to the Validation Report.

Field 12:

6 - CHANGE CONTROLS

It must contain the forecast of the actions to be taken for the execution of a change or correction of the validated transport process during or after the end of the validation.

Anvisa recommendations!

ANNEX II - Transport Validation Result Report Template

Field 1 : **Institution logo**

The placement of the institution's logo is recommended.

Field 2: **Document title**

This field must contain the name given to the document, such as: “Transport Validation Protocol …”.

Field 3: **Version**

This field must contain the version number of the document.

Field 4: **Document number**

This field must contain the number or alphanumeric code to be defined by the institution.

Field 5: **Prepared by**

This field must contain the name and position of the person or persons who prepared the document. The date on which the preparation of the document was completed, with its respective approval, must also be included.

Name: _____ Name: _____

Position: _____ Position: _____

Data: _____ Data: _____

Field 6: **Approved by**

This field must contain the name and position of the person or persons who approved the document. The date on which the approval of the document was completed must also be included.

Name: _____ Name: _____

Position: _____ Position: _____

Data: _____ Data: _____

institution logo	Institution Name				
	Title: Transport Validation Protocol for ...				
	Number:	Revision:	Approval date:	Effective date:	Sheet 2/3

Field 7:

1. INTRODUCTION

In this field, the document in question must be presented, referring to its respective Validation Protocol.

Field 8:

2 – OBJECTIVES

This field must contain the general objective and the specific objects defined in the Validation Protocol.

Field 9:

3 - SCOPE AND RESPONSIBILITIES

In this field, detail the areas and people of the institution who were involved in carrying out the validation study. Responsibilities related to the validation study must be described in this field.

Field 10:

4 - REFERENCES

Describe in this field the documents consulted for the preparation of this document, as well as those used during the execution of the transport validation.

Field 11:

5 - PROCEDURE

This field was subdivided into sub-items, and it is up to the service to decide the most appropriate form for its process.

5.1 - Transport processes

In this field, the previously established transport process must be described or the document where such information is found must be referenced. Information related to the execution of the study must also be included, such as the date on which the study was carried out and the number of runs performed, as well as their respective packaging configurations. Any unusual occurrence must be reported and its impact must be evaluated, as well as any actions taken during the course of the study must be described.

5.2 - Data and results

Present all data and results obtained during the study against the acceptance criteria previously defined in the Validation Protocol. Tables can be useful for better visualization of data. Statistical treatment of the data can also be used, if its application is possible.

<table>
<tr><td rowspan="3">institution logo</td><td colspan="5">Institution Name</td></tr>
<tr><td colspan="5">Title: Transport Validation Protocol for ...</td></tr>
<tr><td>Number:</td><td>Revision:</td><td>Approval date:</td><td>Effective date:</td><td>Sheet 2/3</td></tr>
</table>

Field 12:

6 - CONCLUSION

In this field, the conclusion on the validation of transport must be described, that is, it must be clearly written whether the transport process is validated or not, with the relevant considerations about the process. Determinations, recommendations and possible adjustments may also be contemplated in this field.

Field 13:

7 - CHANGE CONTROLS

It should include any change control process carried out during or after the end of the validation. Each of them should contain a section referring to the impact assessment.

Field 14:

8 - REVALIDATION

Generally, the procedures and criteria for carrying out a revalidation are included in the Master Validation Plan provided for in the Service Validation Policy; if it deems pertinent, however, the service may include such information in this field.

17. REFERENCES

1. BRAZILIAN ASSOCIATION OF TECHNICAL STANDARDS (ABNT). NBR 14785. *Clinical Laboratory* - Safety Requirements. 2001.

2. BRAZIL. National Civil Aviation Agency (Anac). *Air Transport of Dangerous Goods* – Infectious Substances. Training Center – Anac, 2012.

9, 2009. GMC Resolution 50/08. *Common Technical Regulation for the Transport of Infectious Substances and Biological Samples between Mercosur States Parties.*

4. FOOD AND DRUG ADMINISTRATION (FDA). CFR - *Code of Federal Regulations Title 21.* Part 600. Biological Products: General. Subpart B-Establishment Standards Sec. 600.15 Temperatures during shipment. 21CFR600.15, 2011.

5. MAJIC, Z. et al. Research of the Influence of Air Transportation on Blood Sample Quality. Promet – *Traffic & Transportation,* v. 23, n. 6, p. 431-442, 2011.

6. INTERNATIONAL CIVIL AVIATION ORGANIZATION (ICAO). Document 9284-AN/905 Technical Instructions for *the Safe Transport of Dangerous Goods by Air Mode* – Technical Instructions for Safe Transport of Dangerous Goods by Air.

7. WORLD HEALTH ORGANIZATION (WHO). *Guidance on regulations for the transport of infectious substances 2013–2014* (HSE/GCR/2012.12).

_____. *Transport of Infectious Substances 2004* 8. (CDS/CSR/LYO/2004.9). General information on the amendments to the 13th revision of the United Nations Model Regulations regarding the transport of infectious substances.

9. _____. *Substance Transport Training infectious.* Course for Senders. 2011.

10. _____. Recommendations for the production, control and regulation of human plasma for fractionation. *Technical Report Series* n. 941, 2007.

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