Guidelines for laboratories producing data for AMAP Human Health Studies

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1 Introduction
AMAP's current objective is "providing reliable and sufficient information on the status of, and threats to, the Arctic environment, and providing scientific advice on actions to be taken in order to support Arctic governments in their efforts to take remedial and preventive actions relating to contaminants" (AMAP, 2008). Long-term monitoring and trend analysis of contaminant levels in Arctic populations is a crucial component of this objective. Blood is the medium of choice for biological monitoring of contaminants as it accurately reflects the body burden of metals as well as organic contaminants, and is universally available from all members of a population. For lipophilic compounds, which include most POPs, blood levels, expressed on a lipid basis, are well-correlated with levels in other compartments such as stored fat and breast milk. To ensure the comparability of data obtained from different countries requires that adequately sampled and preserved blood specimens be obtained. Laboratories performing the analyses must demonstrate equivalence of results. Data generated must be analyzed using equivalent statistical design and conventions.

2 General Principles
Laboratories that report data for AMAP HH purposes must fulfill two essential requirements:

1) Demonstrate their capacity to reliably produce suitable analytical data over long periods of time. This includes adequate infrastructure, equipment, trained personnel, and appropriate administrative and operating procedures, all of which can be verified by onsite inspection. Accreditation by the laboratory to a recognized standard, such as ISO 17025, (ISO 2005) is the preferred means of demonstrating that the laboratory is in a position to produce quality data.

2) Demonstrate that they are actually producing data of the required quality, ie accurate within a prespecified margin of error, and reproducible over time.

Various analytical procedures may be used, as long as they have been validated as to their suitability and reliability.

Proper sampling, conservation and transportation of specimens are essential to ensure quality of results. The use of a standard sampling protocol for all studies is recommended.
3 Content

3.1 Ensuring Adequate Laboratory Capacity to Produce Quality Data

Contaminant data reported by laboratories are used to evaluate temporal and geographic trends in population exposure. Thus laboratories providing the data must be able to reliably produce accurate data.

To do so requires that the laboratory possesses the necessary infrastructure, equipment, personnel within an appropriate administrative environment. Rather than setting out specific requirements for AMAP HH contributing laboratories, it makes more sense to use mechanisms already in place, namely nationally and internationally recognized accreditation standards. The best known and most recognized accreditation standard for analytical laboratories is ISO/IEC 17025:2005 (ISO 2005) and its derived version for medical laboratories ISO 15189:2007 (ISO 2007). Accreditation bodies in each country are responsible for accrediting laboratories to the standards. Both standards specifically address factors relevant to a laboratory’s ability to produce precise, accurate test data, including:

- Technical competency of staff
- Validity and appropriateness of the methods
- Traceability of measurements and calibrations to national standards
- Appropriate application of measurement uncertainty
- Suitability, calibration, and maintenance of test equipment
- Testing environment
- Sampling, handling, and transportation of test items
- Quality assurance of test, inspection, or calibration data

Accreditation to ISO/IEC 17025 also covers the quality systems elements addressed in ISO 9001 certification that are specifically relevant to laboratories.

Other accreditation standards exist. As an example, US medical laboratories must be certified under CLIA (CLIA 2004). This standard is much more focused on actual lab operations, rather than overall quality system and laboratory management, and it also addresses concerns that are specific to the US situation.

It is strongly recommended that AMAP HH contributing laboratories be accredited under a recognized standard. Although ISO 17025 and/or 15189 are the preferred standards, national standards may also be acceptable.

For laboratories not yet accredited, successful participation in an international external quality assurance scheme should be considered a minimum requirement.

3.2 Pre-analytical Aspects

“The quality of a result is only as good as the sample received in the laboratory” is an oft-quoted maxim among analytical chemists. The appropriate selection of individuals to be sampled within a population is also essential but outside the scope of these guidelines.
As to the sampling process, every effort should be made to ensure that specimens are adequately collected, conserved and transported to the analytical laboratory. The following recommended practices draw on the multi-decade experience of the Centre de Toxicologie and the Centers for Disease Control in measuring trace levels of contaminants in human epidemiological studies. We recommend that all participating researchers adhere strictly to these practices. If any changes are made (e.g., using a different type of blood collection tube) they must be documented and validated prior to undertaking the sampling.

### 3.2.1 Collection of samples

The measurement of POPs may be performed in either blood plasma or blood serum. Briefly, blood is drawn into the prescribed vacuum tube using an approved collection system. Plasma and/or serum are then obtained by appropriate treatment. Portions of the plasma or serum are then transferred to specified containers for conservation and shipment to the analytical laboratory. All equipment and containers used must have been verified to ensure they are exempt from contamination. Samples must be adequately labeled, using a predetermined labeling scheme. Details are given in Annex 1.

### 3.2.2 Biosafety issues

Human blood, as well as other body fluids such as semen and maternal milk may contain viral and bacterial pathogens and are thus vectors for the transmission of diseases, including AIDS and various forms of hepatitis.

Since the emergence of AIDS in the early 1980s, awareness of the health risk from blood has grown, and as a consequence, sound procedures have been promulgated to ensure that health workers are protected from infection. Known as “Universal precautions” these procedures are mandated by national and international bodies.

For example, the US Centers for Disease Control and Prevention (CDC) defines “Universal precautions” as a set of precautions designed to prevent transmission of human immunodeficiency virus (HIV), hepatitis B virus (HBV), and other bloodborne pathogens when providing first aid or health care. Under universal precautions, blood and certain body fluids of all patients are considered potentially infectious for HIV, HBV and other bloodborne pathogens. (CDC 1987, CDC 1988)

Universal precautions apply to blood, other body fluids containing visible blood, semen, and vaginal secretions. Universal precautions also apply to tissues and to the following fluids: cerebrospinal, synovial, pleural, peritoneal, pericardial, and amniotic fluids. Universal precautions do not apply to feces, nasal secretions, sputum, sweat, tears, urine, and vomitus unless they contain visible blood. Universal precautions do not apply to saliva except when visibly contaminated with blood or in the dental setting where blood contamination of saliva is predictable. Whereas universal precautions do not apply to human breast milk, gloves may be worn by health-care workers in situations where exposures to breast milk might be frequent, for example, in breast milk banking.
Universal precautions involve the use of protective barriers such as gloves, gowns, aprons, masks, or protective eyewear, which can reduce the risk of exposure of the health care worker’s skin or mucous membranes to potentially infective materials. In addition, under universal precautions, it is recommended that all health care workers take precautions to prevent injuries caused by needles, scalpels, and other sharp instruments or devices.

Detailed procedures for implementing universal precautions are shown in Annex 2.

3.2.3 Transportation of samples

Once collected and processed, plasma or serum samples may be kept at 4°C for up to one week prior to being sent to the analytical laboratory. They may also be conserved at -20°C for longer periods (several months). No conservation agent is needed nor should any be added because of the risk of contamination. For transportation, appropriate containers must be used, with an approved triple-barrier system to contain any spill in case of breakage. A packing list identifying each sample must be included. Shipment should be effected via a rapid courier service, using a package tracking system. If crossing international borders, the necessary documentation should be prepared to ensure unhindered passage. More details are given in Annex 3.

3.2.4 Receipt and conservation of samples in the analytical laboratory

Upon arrival in the laboratory, the package should be immediately opened and examined to ensure that samples are in good condition and that the packing list corresponds to the actual samples present. Samples should then be logged into the laboratory information management system and kept refrigerated (short term) or frozen until needed for analysis. The sender should be informed of sample receipt, as well as of any problems.

3.3 Analytical Procedures

It is important to point out that laboratory methods are not static but evolve constantly as laboratories strive to achieve better performance, aspects of which include accuracy, precision, selectivity and sensitivity. This is made possible notably through the ongoing improvement in analytical technology. Furthermore, different laboratories do not all have access to the same instrumentation, but may be perfectly capable of producing acceptable results. It is thus more rational to specify performance targets and monitor the performance of the laboratories. Therefore, no specific recommendations as to the analytical methodology should nor will be made. Instead minimum requirements should be specified for the following aspects of performance:

- Detection capacity
- Specificity (ability to distinguish individual analytes in a mixture)
- Reproducibility of results
- Accuracy of results

Currently achievable detection limits for selected POPs are given in Annex 4. As technology evolves, it is expected that lower detection limits may be reached.
3.3.1 Expressing results on a lipid weight basis

Levels of POPs in human serum or plasma are routinely reported on a lipid-adjusted basis, as a means of reducing intra- and inter-individual variations. The rationale for this adjustment is that POPs levels in circulating lipids are in equilibrium with those in stored body fat. To ensure that lipid measurements are accurate it is recommended that enzymatic, rather than gravimetric methods be used. Enzymatic methods are performed on a routine basis by clinical laboratories worldwide using commercially available kits. These methods require small quantities of plasma or serum (<0.1 mL) to measure two major categories of circulating lipids, total cholesterol and triglycerides. It has recently been shown (Bernert et al, 2007) that summing these two components using a simple formula could provide a valid estimate of total serum lipid. It is recommended that laboratories determine total lipids using this formula.

3.4 Quality control and quality assurance

Adequate quality control procedures will ensure and document that analytical output is reproducible over time. Laboratories can only be accredited if they have demonstrated that adequate quality control procedures have been implemented. This should ensure that no data is produced by the laboratory unless the analytical procedures are in control, implying that the measurement uncertainty is within the predetermined criteria. The internal quality control data record should be made available to clients upon request.

Quality assurance serves to ensure and document that laboratory results are accurate. AMAP HH reporting laboratories must participate regularly and successfully in at least one ongoing external quality assessment scheme in order for their results to be acceptable.

3.4.1 Available External Quality Assurance Schemes (EQAS)

For POPs in human blood, the following international EQAS are available:

- The AMAP Ring Test, Centre de Toxicologie, INSPQ, Quebec, Canada (INSPQ, 2009)
- The German External Quality Assessment Scheme (Institute and Outpatient Clinic of Occupational, Social and Environmental Medicine of the Friedrich-Alexander-University Erlangen-Nuremberg) (GEQUAS, 2009)

For heavy metals in human biological fluids, international EQAS include:

- The UK Trace Element Quality Assessment Scheme (University of Surrey, Guilford, UK)
- The German External Quality Assessment Scheme (Institute and Outpatient Clinic of Occupational, Social and Environmental Medicine of the Friedrich-Alexander-University Erlangen-Nuremberg)
- The Interlaboratory Comparison Program for Metals in Biological Matrices (PCI) Centre de toxicologie, INSPQ, Quebec, Canada
- The Quebec Multipetal External Quality Assessment Scheme (QMEQAS) Centre de toxicologie, INSPQ, Quebec, Canada
The above lists of EQAS are known to accept participants without restriction as to national or geographic origin. Other schemes with a regional or national scope also exist and may be suitable for the purpose of demonstrating the accuracy of participating laboratories.

3.4.2 Performance criteria

Performance criteria vary among EQAS, reflecting their different purposes, origins and history. They are usually based on the clinical or epidemiological requirements, taking into account analytical feasibility. In the AMAP Ring Test, results within ±20% of the target value are considered to be excellent. Results within ±40% are acceptable.

The German EQAS considers participant variability within an EQA event to set the acceptable range of values, thus criteria will depend on the proficiency of participants within that event. Acceptability criteria for POPS generally range between ±20 and ±35% of the target value.

3.5 Post-analytical Data Handling and Reporting

Within the laboratory, the post-analytical activities consist of interpreting the data from the raw instrument output, synthesizing the results and providing an adequate report to the client. Within a diagnostic setting, the laboratory should provide a range of normal or expected values, and may provide guidance to the client if measured levels are outside this range. In the case of epidemiological studies, data must be provided electronically, in a predetermined format, as agreed-upon with the client. Detection limits must be clearly specified for samples reported as lower than the limit of detection. Analytical uncertainty is an important factor which should be determined by the laboratory for each type of measurement, and available if requested by the client.

4 References

AMAP 2008: www.amap.no


CDC 1988 : Centers for Disease Control Perspectives in Disease Prevention and Health Promotion Update: Universal Precautions for Prevention of Transmission of Human Immunodeficiency Virus, Hepatitis B Virus, and Other Bloodborne Pathogens in Health-Care Settings MMWR June 24, 1988 / 37(24);377-388
CDC 2005: National Health and Nutrition Examination Survey Laboratory Procedures Manual:  
(http://www.cdc.gov/nchs/data/nhanes/nhanes_05_06/LAB.pdf)

CLIA 2004:  (http://wwwn.cdc.gov/clia/regs/toc.aspx)

GEQUAS 2009: The German External Quality Assessment Scheme For Analyses In Biological Materials (http://www.g-equas.de)

INSPQ 2009: The AMAP Ring Test for Persistent Organic Pollutants in Human Serum  (http://www.inspq.qc.ca/ctq/page/amap/default.asp?Lg=en)

ISO 2005: General requirements for the competence of testing and calibration laboratories, International organization for standardization, Geneva (www.iso.org)

ISO 2007: Medical laboratories -- Particular requirements for quality and competence, International organization for standardization, Geneva (www.iso.org)
5 Annexes

5.1 Annex 1: Recommendations for the collection, handling, and conservation of blood, including plasma and serum, for the purpose of environmental contaminant measurement

Adherence to these recommendations will ensure that the collected sample is adequate, exempt from external contamination and well-conserved prior to shipment to the laboratory. Because the sought-for analytes are present in extremely low concentrations, it is particularly important to use adequate, contamination-free collection containers and equipment, including pipettes and vials for transferral and storage of plasma or serum.

It is recognized that availability of specific blood collection equipment and containers may vary from country to country. If equipment/containers different from those recommended are to be used, they must be adequately tested for contamination by the analytical laboratory prior to their use.

An example of a sampling protocol for plasma is given at the end of this Annex. For a more comprehensive example, the reader is referred to the laboratory procedure manual used for the US CDC’s 2005 National Health and Nutrition Examination Survey (NHANES 2005).

Phlebotomy (blood collection)

The act of blood collection must be performed by trained and licensed personnel (typically nurses or laboratory technologists) observing universal precautions. General references for proper practice are given below (CAP 2002, NCCLS 2004). Despite their training, phlebotomists may not be aware of the particular needs for trace contaminant analysis. It is thus important that they familiarize themselves with the specific requirements of the study (type of tube, order of draw, etc).
**Sampling equipment and containers**

It is recommended that a commercially-available vacuum-tube and barrel system (eg Vacutainer® - see Figure 1) system from Becton-Dickinson or a closed blood collection system (eg Sarstedt S-Monovette® - see Figure 2) be used. Do not use glass syringes. The specific tube to be used, as well as subsequent specimen handling, will depend on the analytes to be measured. A list of appropriate containers can be found at the end of this document.

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**Figure 1 : Vacutainer® System**

**Figure 2 : Monovette® System**

**Specimen Identification**

*Adequate identification of specimens is a crucial preanalytical step*

Two distinct situations may arise: For regular patient diagnostic, identity of patient is shown on the tube label. For epidemiological studies, the usual practice is that tubes are anonymised, i.e., identified only by a code number to ensure that the laboratory is blinded as to the origin and identity of samples.

1. **Diagnostic setting (individual patient):**
   - The phlebotomist must identify each patient specimen immediately after sampling, and in the presence of the patient.
   - The sample identification label must be sturdily affixed to the tube and minimally contain the following information.
     - Patient name
     - Date and time of sampling
     - Initials of phlebotomist
2 Population and epidemiological studies

- The phlebotomist is provided with a list of study subjects with their corresponding study code.
- The sample identification label must be sturdily affixed to the tube and contain the following information.
  - Unique study ID number
  - Date and time of sampling
  - Initials of phlebotomist

Sample volume

The volume of blood required will be in the range of 5-10 ml (or 2.5-5 ml plasma/serum) depending on the number of analytes to be determined. Only in extreme cases as with the analysis of dioxins; 20 ml of plasma is required.

Sample handling

Additional handling of sample is often necessary, e.g., separation of blood into plasma or serum, aliquotting into various containers, etc. To obtain whole, anticoagulated blood, gently mix anticoagulant and blood by inverting collecting tube 7-8 times immediately after draw. To obtain plasma, likewise gently mix anticoagulant and blood by inverting collecting tube 7-8 times immediately after draw, then separate plasma from cells by centrifugation within 20 minutes. To obtain serum, allow blood to clot at ambient temperature and then, separate serum from clot by centrifugation within 20-30 minutes of collection. Do not use a clot activator tube, as this may introduce contamination. Plasma and serum are transferred into pre cleaned vials using appropriate pipettes, before capping and freezing.

Conservation

Place specimens in refrigerator (4°C) as soon as possible. Specimens may be kept for a week at 4° C, prior to shipping to laboratory. For longer conservation times (several months) freeze to and keep at -20°C. Whole blood sample tubes must be frozen lying horizontally to avoid breakage. They can subsequently be kept vertically if more convenient.

Example: A protocol for blood collection, sample processing and shipping for POPs in plasma following a standard phlebotomy protocol observing universal precautions

Blood collection

1. The phlebotomist is provided with a list of study respondents scheduled for sampling, and if not already filled out, consent forms to be read and signed by respondents. The list may also serve as a cover sheet to accompany samples, or alternately a blank cover sheet can be provided to be filled out.
2. The phlebotomist will first confirm the identity of the study respondent by asking the respondent to verify their name, date of birth and signing of the consent form.

3. The phlebotomist will label a 10 mL BD 366643 EDTA-containing Vacutainer tube with his/her initials, the date and respondent’s identification number. The same patient information will be added to the cover sheet.

4. The respondent will be asked to sit in a suitable chair and designate which arm he/she would prefer for the venipuncture procedure.

5. An accessible vein will be located and the puncture site will be cleansed two times with an alcohol wipe; a tourniquet will be applied to the arm.

6. The vein will be punctured using a 21 gauge, multiple sample needle with direct luer adapter.

7. Blood will be collected in labeled Vacutainer tube.

8. Immediately after collection, tube will be gently inverted 7-8 times to ensure mixing of the anticoagulant and then cooled slowly to 4°C (tubes should not be placed directly on ice to avoid hemolyzing the sample).

9. The needle will be withdrawn and the puncture site will be covered with sterile gauze and a band-aid.

10. Used needles and tube holders will be discarded into a biohazardous waste container for later disposal.

11. The respondent will be reminded to keep pressure on the puncture site for several minutes to prevent bruising.

12. Any adverse reaction will be recorded on the cover sheet by the phlebotomist for eventual follow-up.

13. The cover sheet will then be placed into the specimen transport bag and the package will be transported to the medical laboratory for processing. (note: in some circumstances, sample processing may be carried out at the same site)

14. When the sample is dropped off at the medical laboratory the phlebotomist will be required to sign a chain of custody form indicating date, time and name of person relinquished to for processing. (note: chain of custody requirements may vary).

Sample Processing Procedure (following phlebotomy)

Depending on local circumstances, sample processing may be carried out by the same personnel (e.g. small field operation) or by other staff (e.g., hospital setting, where samples would be processed by the hospital medical laboratory)

1. Samples processed at the medical laboratory will first be checked that the sample identification number on the received tubes matches the identification number on the included cover sheet.

2. A set of labels will be prepared for the plasma vials (see 4, below), with the same sample identification numbers.
3. Anticoagulated blood tubes will be centrifuged at 1,500 X g for 20 minutes.

4. Using a polyethylene pipet (Baxter # P5214-10), the plasma will then be transferred the plasma into a 7 mL screw cap precleaned glass vial sealed with a Teflon disc. (Supelco # 2-7341).

5. Collected plasma will be stored in a secure freezer compartment at - 20 °C (or lower) until shipment.

6. Used tubes, pipettes and remaining red matter will be disposed of appropriately.

7. Accumulated cover sheets will be stored in a secure location until transmitted to appropriate study authorities.

8. Accumulated chain of custody forms will be stored until plasma specimens are shipped to the analytical laboratory.

9. Copies of the chain of custody form will be included with the samples when shipped to the analytical laboratory.

Sample Shipment

Specific shipment procedures may vary depending on local circumstances and regulations. Shipment procedures should ensure sample integrity, as well as rapid and traceable dispatch to the analytical laboratory.

1. At the time of packing, chain of custody forms will be signed out by the packing staff.

2. Frozen samples will be appropriately packed into an insulated cooler.

3. Samples will be shipped by a reliable courier service.

4. Tracking number will be communicated to receiving laboratory, who will notify sending laboratory on sample reception.

References


NHANES 2005 Laboratory Procedures Manual, 883 pp
http://www.cdc.gov/nchs/data/nhanes/nhanes_05_06/LAB.pdf
5.2 Annex 2: Universal precautions

This is the integral document published by CDC in MMWR Supplements August 21, 1987 / 36(SU02);001. Sections specific to sample collection, transportation and laboratory handling are highlighted in yellow.

Since medical history and examination cannot reliably identify all patients infected with HIV or other blood-borne pathogens, blood and body-fluid precautions should be consistently used for ALL patients. This approach, previously recommended by CDC (3,4), and referred to as "universal blood and body-fluid precautions" or "universal precautions," should be used in the care of ALL patients, especially including those in emergency-care settings in which the risk of blood exposure is increased and the infection status of the patient is usually unknown (20).

1. All health-care workers should routinely use appropriate barrier precautions to prevent skin and mucous-membrane exposure when contact with blood or other body fluids of any patient is anticipated. Gloves should be worn for touching blood and body fluids, mucous membranes, or non-intact skin of all patients, for handling items or surfaces soiled with blood or body fluids, and for performing venipuncture and other vascular access procedures. Gloves should be changed after contact with each patient. Masks and protective eyewear or face shields should be worn during procedures that are likely to generate droplets of blood or other body fluids to prevent exposure of mucous membranes of the mouth, nose, and eyes. Gowns or aprons should be worn during procedures that are likely to generate splashes of blood or other body fluids.

2. Hands and other skin surfaces should be washed immediately and thoroughly if contaminated with blood or other body fluids. Hands should be washed immediately after gloves are removed.

3. All health-care workers should take precautions to prevent injuries caused by needles, scalpels, and other sharp instruments or devices during procedures; when cleaning used instruments; during disposal of used needles; and when handling sharp instruments after procedures. To prevent needlestick injuries, needles should not be recapped, purposely bent or broken by hand, removed from disposable syringes, or otherwise manipulated by hand. After they are used, disposable syringes and needles, scalpel blades, and other sharp items should be placed in puncture-resistant containers for disposal; the puncture-resistant containers should be located as close as practical to the use area. Large-bore reusable needles should be placed in a puncture-resistant container for transport to the reprocessing area.

4. Although saliva has not been implicated in HIV transmission, to minimize the need for emergency mouth-to-mouth resuscitation, mouthpieces, resuscitation bags, or other ventilation devices should be available for use in areas in which the need for resuscitation is predictable.

5. Health-care workers who have exudative lesions or weeping dermatitis should refrain from all direct patient care and from handling patient-care equipment until the condition resolves.

6. Pregnant health-care workers are not known to be at greater risk of contracting HIV infection than health-care workers who are not pregnant; however, if a health-care worker develops HIV infection during pregnancy, the infant is at risk...
of infection resulting from perinatal transmission. Because of this risk, pregnant health-care workers should be especially familiar with and strictly adhere to precautions to minimize the risk of HIV transmission. Implementation of universal blood and body-fluid precautions for ALL patients eliminates the need for use of the isolation category of "Blood and Body Fluid Precautions" previously recommended by CDC (7) for patients known or suspected to be infected with blood-borne pathogens. Isolation precautions (e.g., enteric, "AFB" (7)) should be used as necessary if associated conditions, such as infectious diarrhea or tuberculosis, are diagnosed or suspected.

Precautions for Invasive Procedures

In this document, an invasive procedure is defined as surgical entry into tissues, cavities, or organs or repair of major traumatic injuries 1) in an operating or delivery room, emergency department, or outpatient setting, including both physicians' and dentists' offices; 2) cardiac catheterization and angiographic procedures; 3) a vaginal or cesarean delivery or other invasive obstetric procedure during which bleeding may occur; or 4) the manipulation, cutting, or removal of any oral or perioral tissues, including tooth structure, during which bleeding occurs or the potential for bleeding exists. The universal blood and body-fluid precautions listed above, combined with the precautions listed below, should be the minimum precautions for ALL such invasive procedures.

1. All health-care workers who participate in invasive procedures must routinely use appropriate barrier precautions to prevent skin and mucous-membrane contact with blood and other body fluids of all patients. Gloves and surgical masks must be worn for all invasive procedures. Protective eyewear or face shields should be worn for procedures that commonly result in the generation of droplets, splashing of blood or other body fluids, or the generation of bone chips. Gowns or aprons made of materials that provide an effective barrier should be worn during invasive procedures that are likely to result in the splashing of blood or other body fluids. All healthcare workers who perform or assist in vaginal or cesarean deliveries should wear gloves and gowns when handling the placenta or the infant until blood and amniotic fluid have been removed from the infant's skin and should wear gloves during post-delivery care of the umbilical cord.

2. If a glove is torn or a needlestick or other injury occurs, the glove should be removed and a new glove used as promptly as patient safety permits; the needle or instrument involved in the incident should also be removed from the sterile field.

Precautions for Dentistry *

Blood, saliva, and gingival fluid from ALL dental patients should be considered infective. Special emphasis should be placed on the following precautions for preventing transmission of blood-borne pathogens in dental practice in both institutional and non-institutional settings.

1. In addition to wearing gloves for contact with oral mucous membranes of all patients, all dental workers should wear surgical masks and protective eyewear or chin-length plastic face shields during dental procedures in which splashing or spattering of blood, saliva, or gingival fluids is likely. Rubber dams, high-speed
evacuation and proper patient positioning, when appropriate, should be utilized to minimize generation of droplets and spatter.

2. Handpieces should be sterilized after use with each patient, since blood, saliva, or gingival fluid of patients may be aspirated into the handpiece or waterline. Handpieces that cannot be sterilized should at least be flushed, the outside surface cleaned and wiped with a suitable chemical germicide, and then rinsed. Handpieces should be flushed at the beginning of the day and after use with each patient. Manufacturers' recommendations should be followed for use and maintenance of waterlines and check valves and for flushing of handpieces. The same precautions should be used for ultrasonic scalers and air/water syringes.

3. Blood and saliva should be thoroughly and carefully cleaned from material that has been used in the mouth (e.g., impression materials, bite registration), especially before polishing and grinding intra-oral devices. Contaminated materials, impressions, and intra-oral devices should also be cleaned and disinfected before being handled in the dental laboratory and before they are placed in the patient's mouth. Because of the increasing variety of dental materials used intra-orally, dental workers should consult with manufacturers as to the stability of specific materials when using disinfection procedures.

4. Dental equipment and surfaces that are difficult to disinfect (e.g., light handles or X-ray-unit heads) and that may become contaminated should be wrapped with impervious-backed paper, aluminum foil, or clear plastic wrap. The coverings should be removed and discarded, and clean coverings should be put in place after use with each patient.

Precautions for Autopsies or Morticians' Services

In addition to the universal blood and body-fluid precautions listed above, the following precautions should be used by persons performing postmortem procedures:

1. All persons performing or assisting in postmortem procedures should wear gloves, masks, protective eyewear, gowns, and waterproof aprons.
2. Instruments and surfaces contaminated during postmortem procedures should be decontaminated with an appropriate chemical germicide.

Precautions for Dialysis

Patients with end-stage renal disease who are undergoing maintenance dialysis and who have HIV infection can be dialyzed in hospital-based or free-standing dialysis units using conventional infection-control precautions (21). Universal blood and body-fluid precautions should be used when dialyzing ALL patients.

Strategies for disinfecting the dialysis fluid pathways of the hemodialysis machine are targeted to control bacterial contamination and generally consist of using 500-750 parts per million (ppm) of sodium hypochlorite (household bleach) for 30-40 minutes or 1.5%-2.0% formaldehyde overnight. In addition, several chemical germicides formulated to disinfect dialysis machines are commercially available. None of these protocols or procedures need to be changed for dialyzing patients infected with HIV.

Patients infected with HIV can be dialyzed by either hemodialysis or peritoneal dialysis and do not need to be isolated from other patients. The type of dialysis treatment (i.e.,
hemodialysis or peritoneal dialysis) should be based on the needs of the patient. The
dialyzer may be discarded after each use. Alternatively, centers that reuse dialyzers
<i.e. a specific single-use dialyzer is issued to a specific patient, removed, cleaned,
disinfecte, and reused several times on the same patient only</i> may include HIV-
infected patients in the dialyzer-reuse program. An individual dialyzer must never be
used on more than one patient.

**Precautions for Laboratories**

Blood and other body fluids from ALL patients should be considered infective. To
supplement the universal blood and body-fluid precautions listed above, the following
precautions are recommended for health-care workers in clinical laboratories.

1. All specimens of blood and body fluids should be put in a well-constructed
container with a secure lid to prevent leaking during transport. Care should be
taken when collecting each specimen to avoid contaminating the outside of the
container and of the laboratory form accompanying the specimen.

2. All persons processing blood and body-fluid specimens (e.g., removing tops from
vacuum tubes) should wear gloves. Masks and protective eyewear should be
worn if mucous-membrane contact with blood or body fluids is anticipated.
Gloves should be changed and hands washed after completion of specimen
processing.

3. For routine procedures, such as histologic and pathologic studies or
microbiologic culturing, a biological safety cabinet is not necessary. However,
biological safety cabinets (Class I or II) should be used whenever procedures are
conducted that have a high potential for generating droplets. These include
activities such as blending, sonicating, and vigorous mixing.

4. Mechanical pipetting devices should be used for manipulating all liquids in the
laboratory. Mouth pipetting must not be done.

5. Use of needles and syringes should be limited to situations in which there is no
alternative, and the recommendations for preventing injuries with needles
outlined under universal precautions should be followed.

6. Laboratory work surfaces should be decontaminated with an appropriate
chemical germicide after a spill of blood or other body fluids and when work
activities are completed.

7. Contaminated materials used in laboratory tests should be decontaminated
before reprocessing or be placed in bags and disposed of in accordance with
institutional policies for disposal of infective waste (24).

8. Scientific equipment that has been contaminated with blood or other body fluids
should be decontaminated and cleaned before being repaired in the laboratory or
transported to the manufacturer.

9. All persons should wash their hands after completing laboratory activities and
should remove protective clothing before leaving the laboratory. Implementation
of universal blood and body-fluid precautions for ALL patients eliminates the
need for warning labels on specimens since blood and other body fluids from all
patients should be considered infective.
Environmental Considerations for HIV Transmission

No environmentally mediated mode of HIV transmission has been documented. Nevertheless, the precautions described below should be taken routinely in the care of ALL patients.

Sterilization and Disinfection

Standard sterilization and disinfection procedures for patient-care equipment currently recommended for use (25, 26) in a variety of healthcare settings <<<<including hospitals, medical and dental clinics and offices, hemodialysis centers, emergency-care facilities, and long-term nursing-care facilities <<<<are adequate to sterilize or disinfect instruments, devices, or other items contaminated with blood or other body fluids from persons infected with blood-borne pathogens including HIV (21, 23).

Instruments or devices that enter sterile tissue or the vascular system of any patient or through which blood flows should be sterilized before reuse. Devices or items that contact intact mucous membranes should be sterilized or receive high-level disinfection, a procedure that kills vegetative organisms and viruses but not necessarily large numbers of bacterial spores. Chemical germicides that are registered with the U.S. Environmental Protection Agency (EPA) as "sterilants" may be used either for sterilization or for high-level disinfection depending on contact time.

Contact lenses used in trial fittings should be disinfected after each fitting by using a hydrogen peroxide contact lens disinfecting system or, if compatible, with heat (78 C-80 C {172.4 F-176.0 F}) for 10 minutes.

Medical devices or instruments that require sterilization or disinfection should be thoroughly cleaned before being exposed to the germicide, and the manufacturer's instructions for the use of the germicide should be followed. Further, it is important that the manufacturer's specifications for compatibility of the medical device with chemical germicides be closely followed. Information on specific label claims of commercial germicides can be obtained by writing to the Disinfectants Branch, Office of Pesticides, Environmental Protection Agency, 401 M Street, SW, Washington, D.C. 20460.

Studies have shown that HIV is inactivated rapidly after being exposed to commonly used chemical germicides at concentrations that are much lower than used in practice (27-30). Embalming fluids are similar to the types of chemical germicides that have been tested and found to completely inactivate HIV. In addition to commercially available chemical germicides, a solution of sodium hypochlorite (household bleach) prepared daily is an inexpensive and effective germicide. Concentrations ranging from approximately 500 ppm (1:100 dilution of household bleach) sodium hypochlorite to 5,000 ppm (1:10 dilution of household bleach) are effective depending on the amount of organic material (e.g., blood, mucus) present on the surface to be cleaned and disinfected. Commercially available chemical germicides may be more compatible with certain medical devices that might be corroded by repeated exposure to sodium hypochlorite, especially to the 1:10 dilution.

Survival of HIV in the Environment
The most extensive study on the survival of HIV after drying involved greatly concentrated HIV samples, i.e., 10 million tissue-culture infectious doses per milliliter (31). This concentration is at least 100,000 times greater than that typically found in the blood or serum of patients with HIV infection. HIV was detectable by tissue-culture techniques 1-3 days after drying, but the rate of inactivation was rapid. Studies performed at CDC have also shown that drying HIV causes a rapid (within several hours) 1-2 log (90%-99%) reduction in HIV concentration. In tissue-culture fluid, cell-free HIV could be detected up to 15 days at room temperature, up to 11 days at 37°C (98.6°F), and up to 1 day if the HIV was cell-associated.

When considered in the context of environmental conditions in healthcare facilities, these results do not require any changes in currently recommended sterilization, disinfection, or housekeeping strategies. When medical devices are contaminated with blood or other body fluids, existing recommendations include the cleaning of these instruments, followed by disinfection or sterilization, depending on the type of medical device. These protocols assume "worst-case" conditions of extreme virologic and microbiologic contamination, and whether viruses have been inactivated after drying plays no role in formulating these strategies. Consequently, no changes in published procedures for cleaning, disinfecting, or sterilizing need to be made.

Housekeeping

Environmental surfaces such as walls, floors, and other surfaces are not associated with transmission of infections to patients or health-care workers. Therefore, extraordinary attempts to disinfect or sterilize these environmental surfaces are not necessary. However, cleaning and removal of soil should be done routinely.

Cleaning schedules and methods vary according to the area of the hospital or institution, type of surface to be cleaned, and the amount and type of soil present. Horizontal surfaces (e.g., bedside tables and hard- surfaced flooring) in patient-care areas are usually cleaned on a regular basis, when soiling or spills occur, and when a patient is discharged. Cleaning of walls, blinds, and curtains is recommended only if they are visibly soiled. Disinfectant fogging is an unsatisfactory method of decontaminating air and surfaces and is not recommended.

Disinfectant-detergent formulations registered by EPA can be used for cleaning environmental surfaces, but the actual physical removal of microorganisms by scrubbing is probably at least as important as any antimicrobial effect of the cleaning agent used. Therefore, cost, safety, and acceptability by housekeepers can be the main criteria for selecting any such registered agent. The manufacturers' instructions for appropriate use should be followed.

Cleaning and Decontaminating Spills of Blood or Other Body Fluids

Chemical germicides that are approved for use as "hospital disinfectants" and are tuberculocidal when used at recommended dilutions can be used to decontaminate spills of blood and other body fluids. Strategies for decontaminating spills of blood and other body fluids in a patient-care setting are different than for spills of cultures or other materials in clinical, public health, or research laboratories. In patient-care areas, visible material should first be removed and then the area should be decontaminated. With
large spills of cultured or concentrated infectious agents in the laboratory, the
contaminated area should be flooded with a liquid germicide before cleaning, then
decontaminated with fresh germicidal chemical. In both settings, gloves should be worn
during the cleaning and decontaminating procedures.

Laundry

Although soiled linen has been identified as a source of large numbers of certain
pathogenic microorganisms, the risk of actual disease transmission is negligible. Rather
than rigid procedures and specifications, hygienic and common-sense storage and
processing of clean and soiled linen are recommended (26). Soiled linen should be
handled as little as possible and with minimum agitation to prevent gross microbial
contamination of the air and of persons handling the linen. All soiled linen should be
bagged at the location where it was used; it should not be sorted or rinsed in patient-
care areas. Linen soiled with blood or body fluids should be placed and transported in
bags that prevent leakage. If hot water is used, linen should be washed with detergent in
water at least 71 C (160 F) for 25 minutes. If low-temperature (less than or equal to 70 C
(158 F)) laundry cycles are used, chemicals suitable for low-temperature washing at
proper use concentration should be used.

Infective Waste

There is no epidemiologic evidence to suggest that most hospital waste is any more
infective than residential waste. Moreover, there is no epidemiologic evidence that
hospital waste has caused disease in the community as a result of improper disposal.
Therefore, identifying wastes for which special precautions are indicated is largely a
matter of judgment about the relative risk of disease transmission. The most practical
approach to the management of infective waste is to identify those wastes with the
potential for causing infection during handling and disposal and for which some special
precautions appear prudent. Hospital wastes for which special precautions appear
prudent include microbiology laboratory waste, pathology waste, and blood specimens
or blood products. While any item that has had contact with blood, exudates, or
secretions may be potentially infective, it is not usually considered practical or necessary
to treat all such waste as infective (23, 26). Infective waste, in general, should either be
incinerated or should be autoclaved before disposal in a sanitary landfill. Bulk blood,
suctioned fluids, excretions, and secretions may be carefully poured down a drain
connected to a sanitary sewer. Sanitary sewers may also be used to dispose of other
infectious wastes capable of being ground and flushed into the sewer.

Implementation of Recommended Precautions

Employers of health-care workers should ensure that policies exist for:

1. Initial orientation and continuing education and training of all health-care workers
   including students and trainees on the epidemiology, modes of
   transmission, and prevention of HIV and other blood-borne infections and the
   need for routine use of universal blood and body-fluid precautions for ALL
   patients.
2. Provision of equipment and supplies necessary to minimize the risk of infection
   with HIV and other blood-borne pathogens.
3. Monitoring adherence to recommended protective measures. When monitoring reveals a failure to follow recommended precautions, counseling, education, and/or re-training should be provided, and, if necessary, appropriate disciplinary action should be considered. Professional associations and labor organizations, through continuing education efforts, should emphasize the need for health-care workers to follow recommended precautions.

Serologic Testing for HIV Infection

Background

A person is identified as infected with HIV when a sequence of tests, starting with repeated enzyme immunoassays (EIA) and including a Western blot or similar, more specific assay, are repeatedly reactive. Persons infected with HIV usually develop antibody against the virus within 6-12 weeks after infection.

The sensitivity of the currently licensed EIA tests is at least 99% when they are performed under optimal laboratory conditions on serum specimens from persons infected for greater than or equal to 12 weeks. Optimal laboratory conditions include the use of reliable reagents, provision of continuing education of personnel, quality control of procedures, and participation in performance-evaluation programs. Given this performance, the probability of a false-negative test is remote except during the first several weeks after infection, before detectable antibody is present. The proportion of infected persons with a false-negative test attributed to absence of antibody in the early stages of infection is dependent on both the incidence and prevalence of HIV infection in a population (Table 1).

The specificity of the currently licensed EIA tests is approximately 99% when repeatedly reactive tests are considered. Repeat testing of initially reactive specimens by EIA is required to reduce the likelihood of laboratory error. To increase further the specificity of serologic tests, laboratories must use a supplemental test, most often the Western blot, to validate repeatedly reactive EIA results. Under optimal laboratory conditions, the sensitivity of the Western blot test is comparable to or greater than that of a repeatedly reactive EIA, and the Western blot is highly specific when strict criteria are used to interpret the test results. The testing sequence of a repeatedly reactive EIA and a positive Western blot test is highly predictive of HIV infection, even in a population with a low prevalence of infection (Table 2). If the Western blot test result is indeterminant, the testing sequence is considered equivocal for HIV infection. When this occurs, the Western blot test should be repeated on the same serum sample, and, if still indeterminant, the testing sequence should be repeated on a sample collected 3-6 months later. Use of other supplemental tests may aid in interpreting of results on samples that are persistently indeterminant by Western blot.

Testing of Patients

Previous CDC recommendations have emphasized the value of HIV serologic testing of patients for: 1) management of parenteral or mucous-membrane exposures of health-care workers, 2) patient diagnosis and management, and 3) counseling and serologic testing to prevent and control HIV transmission in the community. In addition, more recent recommendations have stated that hospitals, in conjunction with state and local
health departments, should periodically determine the prevalence of HIV infection among patients from age groups at highest risk of infection (32).

Adherence to universal blood and body-fluid precautions recommended for the care of all patients will minimize the risk of transmission of HIV and other blood-borne pathogens from patients to health-care workers. The utility of routine HIV serologic testing of patients as an adjunct to universal precautions is unknown. Results of such testing may not be available in emergency or outpatient settings. In addition, some recently infected patients will not have detectable antibody to HIV (Table 1).

Personnel in some hospitals have advocated serologic testing of patients in settings in which exposure of health-care workers to large amounts of patients' blood may be anticipated. Specific patients for whom serologic testing has been advocated include those undergoing major operative procedures and those undergoing treatment in critical-care units, especially if they have conditions involving uncontrolled bleeding. Decisions regarding the need to establish testing programs for patients should be made by physicians or individual institutions. In addition, when deemed appropriate, testing of individual patients may be performed on agreement between the patient and the physician providing care.

In addition to the universal precautions recommended for all patients, certain additional precautions for the care of HIV-infected patients undergoing major surgical operations have been proposed by personnel in some hospitals. For example, surgical procedures on an HIV-infected patient might be altered so that hand-to-hand passing of sharp instruments would be eliminated; stapling instruments rather than hand-suturing equipment might be used to perform tissue approximation; electrocautery devices rather than scalpels might be used as cutting instruments; and, even though uncomfortable, gowns that totally prevent seepage of blood onto the skin of members of the operative team might be worn. While such modifications might further minimize the risk of HIV infection for members of the operative team, some of these techniques could result in prolongation of operative time and could potentially have an adverse effect on the patient.

Testing programs, if developed, should include the following principles:

1. Obtaining consent for testing.
2. Informing patients of test results, and providing counseling for seropositive patients by properly trained persons.
3. Assuring that confidentiality safeguards are in place to limit knowledge of test results to those directly involved in the care of infected patients or as required by law.
4. Assuring that identification of infected patients will not result in denial of needed care or provision of suboptimal care.
5. Evaluating prospectively 1) the efficacy of the program in reducing the incidence of parenteral, mucous-membrane, or significant cutaneous exposures of health-care workers to the blood or other body fluids of HIV-infected patients and 2) the effect of modified procedures on patients.

Testing of Health-Care Workers
Although transmission of HIV from infected health-care workers to patients has not been reported, transmission during invasive procedures remains a possibility. Transmission of hepatitis B virus (HBV) a blood-borne agent with a considerably greater potential for nosocomial spread from health-care workers to patients has been documented. Such transmission has occurred in situations (e.g., oral and gynecologic surgery) in which health-care workers when tested had very high concentrations of HBV in their blood (at least 100 million infectious virus particles per milliliter, a concentration much higher than occurs with HIV infection), and the health-care workers sustained a puncture wound while performing invasive procedures or had exudative or weeping lesions or microlacerations that allowed virus to contaminate instruments or open wounds of patients (33, 34).

The hepatitis B experience indicates that only those health-care workers who perform certain types of invasive procedures have transmitted HBV to patients. Adherence to recommendations in this document will minimize the risk of transmission of HIV and other blood-borne pathogens from health-care workers to patients during invasive procedures. Since transmission of HIV from infected health-care workers performing invasive procedures to their patients has not been reported and would be expected to occur only very rarely, if at all, the utility of routine testing of such health-care workers to prevent transmission of HIV cannot be assessed. If consideration is given to developing a serologic testing program for health-care workers who perform invasive procedures, the frequency of testing, as well as the issues of consent, confidentiality, and consequences of test results as previously outlined for testing programs for patients must be addressed.

Management of Infected Health-Care Workers

Health-care workers with impaired immune systems resulting from HIV infection or other causes are at increased risk of acquiring or experiencing serious complications of infectious disease. Of particular concern is the risk of severe infection following exposure to patients with infectious diseases that are easily transmitted if appropriate precautions are not taken (e.g., measles, varicella). Any health-care worker with an impaired immune system should be counseled about the potential risk associated with taking care of patients with any transmissible infection and should continue to follow existing recommendations for infection control to minimize risk of exposure to other infectious agents (7, 35). Recommendations of the Immunization Practices Advisory Committee (ACIP) and institutional policies concerning requirements for vaccinating health-care workers with live-virus vaccines (e.g., measles, rubella) should also be considered.

The question of whether workers infected with HIV especially those who perform invasive procedures can adequately and safely be allowed to perform patient-care duties or whether their work assignments should be changed must be determined on an individual basis. These decisions should be made by the health-care worker's personal physician(s) in conjunction with the medical directors and personnel health service staff of the employing institution or hospital.

Management of Exposures

If a health-care worker has a parenteral (e.g., needlestick or cut) or mucous-membrane (e.g., splash to the eye or mouth) exposure to blood or other body fluids or has a
cutaneous exposure involving large amounts of blood or prolonged contact with blood especially when the exposed skin is chapped, abraded, or afflicted with dermatitis the source patient should be informed of the incident and tested for serologic evidence of HIV infection after consent is obtained. Policies should be developed for testing source patients in situations in which consent cannot be obtained (e.g., an unconscious patient).

If the source patient has AIDS, is positive for HIV antibody, or refuses the test, the health-care worker should be counseled regarding the risk of infection and evaluated clinically and serologically for evidence of HIV infection as soon as possible after the exposure. The health-care worker should be advised to report and seek medical evaluation for any acute febrile illness that occurs within 12 weeks after the exposure. Such an illness particularly one characterized by fever, rash, or lymphadenopathy may be indicative of recent HIV infection. Seronegative health-care workers should be retested 6 weeks post-exposure and on a periodic basis thereafter (e.g., 12 weeks and 6 months after exposure) to determine whether transmission has occurred. During this follow-up period

- especially the first 6-12 weeks after exposure, when most infected persons are expected to seroconvert exposed health-care workers should follow U.S. Public Health Service (PHS) recommendations for preventing transmission of HIV (36, 37).

No further follow-up of a health-care worker exposed to infection as described above is necessary if the source patient is seronegative unless the source patient is at high risk of HIV infection. In the latter case, a subsequent specimen (e.g., 12 weeks following exposure) may be obtained from the health-care worker for antibody testing. If the source patient cannot be identified, decisions regarding appropriate follow-up should be individualized. Serologic testing should be available to all health-care workers who are concerned that they may have been infected with HIV.

If a patient has a parenteral or mucous-membrane exposure to blood or other body fluid of a health-care worker, the patient should be informed of the incident, and the same procedure outlined above for management of exposures should be followed for both the source health-care worker and the exposed patient.

- General infection-control precautions are more specifically addressed in previous recommendations for infection-control practices for dentistry (8). Additional precautions for research and industrial laboratories are addressed elsewhere (22,23).

References


37. CDC. Provisional Public Health Service inter-agency recommendations for screening donated blood and plasma for antibody to the virus causing acquired immunodeficiency syndrome. MMWR 1985;34:1-5.
5.3 Annex 3: Procedures for the transportation of samples

Introduction
There are three main issues regarding the transportation of biological material:

1. Protection of the safety and health of concerned personnel
2. Preservation of sample integrity
3. Compliance with national and international regulations regarding the transportation of potentially infectious human biological samples

Personnel Protection
To adequately protect personnel, the following controls must be in place prior to transporting any biological materials:

1. Emergency procedures (e.g., contact names and information, spill clean up, disinfection protocols, etc.) must be known to the person carrying the materials.
2. Container must be appropriate for the material being transported.
3. Material must be packed so that it will stay upright during transportation.
4. The containers must be properly labeled.
5. Proper protective clothing must be worn during the packaging of the material.
6. Hands should be washed after handling materials.
7. Open cuts or other wounds should be covered before handling the materials.
8. Aerosol generation must be avoided when handling and packing the materials.
9. The person packaging the material must ensure that the exterior surfaces of each package are free of any potential contamination by the packed material.

Appropriate packaging
Appropriate packaging provides the necessary and sufficient barriers to prevent leakage of the material to the. The use of triple packaging has over the years provided effective containment of infectious substances (WHO, 2004).

Triple packaging comprises:

1. Leakproof primary packagings which are packed in secondary packagings in such a way that they cannot break, be punctured or leak their contents into the secondary packaging,
2. Leakproof secondary packagings secured in strong outer packagings
3. Suitable cushioning material and absorbent materials placed between the primary receptacle(s) and the secondary packaging in a quantity sufficient to absorb the entire contents of the primary receptacle(s) so that any release of liquid substances will not compromise the integrity of the cushioning material or of the outer packaging.

Examples of appropriate triple packaging are shown below.
Packing and Labeling of Clinical Specimens

Packing and Labeling of Infectious Substances
**Shipping:**

Biological specimens must be shipped in a timely manner to avoid degradation of the matrix or the analytes. In the case of environmental contaminants, such as POPs and metals, the analytes are usually very stable, and the principal concern is to ensure integrity of the matrix. Blood, plasma and serum samples can be kept at 4 deg C for at least 2 weeks, and kept frozen at -20 deg C for several weeks. Thus if transit time is less than a week, frozen samples sent in insulated containers will not degrade.

For regional and national transportation, locally known reliable transportation services can be used. For international shipments it is recommended that reliable courier services be used (FedEx, DHL, etc).

Adequate and proper documentation is essential to ensure timely delivery and smooth passage through customs. Detailed procedures are given in IATA guidelines on the transportation of infectious substances (IATA 2008). Customs issues are country-specific and must be addressed locally.

**References:**


IATA 2008 Infectious Substances Shipping Guidelines 2008 ([www.iata.org](http://www.iata.org))
5.4 Annex 4: Recommended detection limits for selected POPs in serum or plasma

These recommendations are based on a collected serum or plasma volume of 2 mL

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<th>Detection limit (µg/L)</th>
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