# The role of laboratory medicine in managing biological risk: proposal for a simple and easy-to-follow protocol for occupational accidents at risk of bloodborne infection

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## SUMMARY

Bloodborne pathogens represent a major hazard for healthcare workers (HCWs) and exposure prevention still represents the primary strategy to reduce the risk of occupational bloodborne pathogen infections, such as hepatitis B (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV). Each healthcare organization should have simple and easy-to-apply operating procedures (OPs), quickly accessible to their personnel, including educational programmes, written protocols for prompt reporting and procedures for correct evaluation, counselling, treatment and follow-up of occupational exposure. From a careful review of literature data and international recommendations, in this study we summarize the recommendations to follow in the event of occupational exposure to HIV, HBV and HCV, also providing tables and a flowchart, that are simple to apply and could be a guide, especially in moments of apprehension caused by the occurrence of an occupational accident due to biohazard, in which important decisions must be taken and appropriate assessments carried out in the shortest possible time. Obviously, for this purpose, the people to be involved in the various processes must appear clearly in each OP, and the forms to be filled in must be easily and promptly accessible at all times.

*Keywords*: Bloodborne infection, healthcare workers, biohazard, prevention, occupational exposure.

## INTRODUCTION

The term "biological risk" (biological hazard, or biohazard,) refers to the possibility for workers to get in direct contact with pathogenic microorganisms capable of transmitting infectious diseases, due to the possible presence or decomposition of organic substances [1].
Occupational accidents from exposure to biological fluids are among the most frequent and serious. In the hospital setting, the health care worker (HCW) may be exposed to different types of biological agents: bacteria, viruses, fungi, protozoa. In particular, the hepatitis B (HBV), hepatitis C (HCV) and human immunodeficiency (HIV) viruses are among the most fearful agents transmitted by the direct contact with blood or other body substances, due to their ability to cause serious and/or persistent infections.
The risk of bloodborne pathogen infection in the healthcare setting can be caused by both direct and indirect factors, such as patient care, wound dressing, cleaning and sterilization of surgical instruments and, last but not least, inappropriate conditions of health care workflow [2].

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Adopting behaviours and wearing the appropriate personal protective equipment to avoid exposure to biological material are certainly the most effective strategies to prevent the transmission of HBV, HCV, and HIV. For this reason, a good program for the prevention of bloodborne infections including written protocols that define the methods of reporting, evaluation, counselling, treatment and follow-up of the exposed person, as well as the description of the most effective post-exposure prophylactic (PEP) measures must necessarily be adopted from each health care facility [3, 4]. It is also necessary that healthcare personnel are well trained in the correct use and disposal of protection devices, in the "risk management" associated with exposure to blood and body fluids, and about the importance of immunization, notification, response and monitoring procedures and any measures to be taken in case of cuts wounds or puncture, etc. [5].
Taking a look at the operating procedures (OPs) available on the websites of different public and private Italian hospitals, we realized that in some cases there is confusion on how to manage occupational accidents, especially due to the lack of standardized national guidelines. Based on a careful review of the literature data, we decide to propose a protocol that is as simple and complete as possible and that can be applied, especially in moments of apprehension such as the occurrence of an occupational accident at biological risk, in which important decisions must be taken and the appropriate assessments implemented in the shortest possible time.

**Risks and methods of transmission**

*HBV*

The hepatitis B virus can be transmitted by an apparent parenteral route (through transfusions of blood or blood products contaminated by the virus or by infected needle or other instruments injuries), sexually, perinatally (from mother to child) and, since the virus can survive in the external environment and in particular in dried blood up to a period of 7 days, it is relatively frequent also its inapparent transmission to unvaccinated people through vehicles contaminated with infected blood and other biological fluids such as saliva, menstrual fluid, vaginal discharge and seminal fluid, which come into contact with minimal skin lesions or mucous membranes [6, 7].

The average risk of developing hepatitis following percutaneous exposure to blood or biological fluids of an infected patient varies according to the serological characteristics of the source patient: it ranges from a risk of 22-31% if the source is positive for HBsAg and for HBeAg at a risk of 1-6% if the source is positive for HBsAg and negative for HBeAg [8]. About the prophylaxis, the 2005 European Guidelines for the management of health professionals occupationally exposed to HBV differ according to the serological status of the operator and the patient source. When necessary, post-exposure prevention with HBV vaccine, specific immunoglobulins or both should be started as soon as possible, preferably within 24 hours from exposure and no later than 1 week [6, 7, 9].

*HCV*

Today, hepatitis C virus transmission mainly occurs by parenteral route and even if some sexual and vertical infections have been documented, these ways of contagion are less frequent. The average risk of HCV transmission after percutaneous exposure is 1.8% (range 0-7%) [10]. Infection is often asymptomatic, and this is the reason why few people are diagnosed during the period of acute infection, that in 75-85% of cases evolves into a chronic form. Unlike the hepatitis B virus, currently there is no prophylaxis: there is no vaccine against hepatitis C and the use of immunoglobulins has not proved to be useful. So, effective prophylactic measures are therefore represented by general hygiene rules, including sterilization of surgical instruments, using disposable materials for aesthetic treatments and protection in sexual intercourse at risk [6, 7].

*HIV*

In recent decades, the effectiveness of antiretroviral therapies has greatly improved the quality of life and survival of people with HIV infection, but to date there is no anti-HIV vaccine or therapy that will allow them to recover from the infection. Prevention therefore remains the only way to protect yourself from this disease [6].
PEP for HIV represents a consolidate measure to prevent the risk of transmission in the healthcare setting and is also widely used for the prevention of sexual transmission [11]. The risk of HIV transmission following a single exposure to an infected source is around 0.3-0.5% on average,

furthermore, a multiplicity of factors relating to the type of exposure, the source and the specific situation of the exposed individual may imply its increase or decrease [12]. In fact, the probability of transmission is correlated with the concentration of HIV in the material to which the individual is exposed, indiscriminately whether it is blood or genital secretion [13]. As all viruses, HIV is unable to replicate autonomously, and it requires the cellular metabolic apparatus. The replicative cycle of HIV is divided into different phases (adhesion; fusion; cell penetration; uncoating; reverse transcription): after entry, the virus replicates in the dendritic cells of the skin and mucous membranes that migrate to the lymph nodes causing a systemic infection within 48 hours. This interval therefore represents a window time of opportunity to block the viral replication mechanism at the site of entry. For this reason, post-exposure therapy with antiviral drugs must be started as soon as possible, preferably within 1-4 hours, and no later than 48 hours after the accident and must be continued for 4 weeks [13].

Nevertheless, there are still limited evidences on the efficacy of PEP in preventing HIV infection and the few studies available seem to evidence that some factors may contribute to the failure of PEP, including drug resistance, exposure to a high viral load and delay in starting the therapy [14-21]. Furthermore, the type of therapy could influence the outcome of PEP based on the combination of two or three drugs, meaning that the need to initiate the PEP must be assessed on a case-by-case evaluation based on a careful risk assessment and in consideration of the potential adverse events that may affect the exposed individual, also considering that these therapies have very high costs and are not free from toxicity. So, it would be advisable to evaluate the cost-effectiveness ratio after a correct counselling [17].

**Route provided for the healthcare worker accidentally exposed to blood or other potentially infected biological material**

Below we propose the route for the HCW accidentally exposed to blood or other potentially infected biological material, considering that the factors that may influence the risk of transmission are essentially three: the type of exposure, the type of material and the status of the source (for details see Tables 1-3).

**Table 1** - Risk of bloodborne virus transmission from infected biological fluids based on type of accident/injury.

| *Risk levels* | *Type of injury* |
|---|---|
| High risk | Deep percutaneous injury<br>Presence of visible blood on the tip or blade of the sharp object<br>Needles used for blood draws or vein infusions |
| Low risk | Superficial wounds, exposure to non-intact skin or mucous membranes<br>Old blades of sharp objects used<br>No visible blood on the tip or blade of a sharp object<br>Needles not used for blood drawing or infusion into a vein (*e.g.* suture or subcutaneous injection needles) |
| No risk | Contact of intact skin with biological fluids<br>Injuries due to needles or other sharp objects not yet used on patient |

Note. Adapted from "HIV, Hepatitis B and Hepatitis C - Management of Health Care Workers Potentially Exposed. NSW Government. Health Procedures". Issue of May 2017. Available at website: https://www1.health.nsw.gov.au/pds/activepdsdocuments/pd2017_010.pdf (last access: 25/08/2020).

**Table 2** - Biological fluids and risk of bloodborne virus transmission.

| *Risk levels* | *Biological fluids* |
|---|---|
| Infectious | Blood<br>Body fluids or other biological materials visibly contaminated with blood |
| Potentially infectious | Amniotic fluid<br>Cerebrospinal fluid<br>Human breast milk<br>Pericardial fluid<br>Peritoneal fluid<br>Pleural fluid<br>Saliva contaminated with blood (*e.g.* associated to dental practices)<br>Seminal fluid<br>Synovial fluid<br>Tissue fluids from wounds or burns<br>Vaginal secretions |
| Not infectious | Nasal discharge*<br>Saliva*<br>Sputum*<br>Feces*<br>Sweat*<br>Tears*<br>Urine*<br>Vomit*<br>*not contaminated with blood |

Note. Adapted from "HIV, Hepatitis B and Hepatitis C - Management of Health Care Workers Potentially Exposed. NSW Government. Health Procedures". Issue of May 2017. Available at website: https://www1.health.nsw.gov.au/pds/activepdsdocuments/pd2017_010.pdf (last access: 25/08/2020).

**Table 3** - Risk assessment based on the type of "source".

| *Risk levels* | *Source* |
|---|---|
| High risk | Source known to be infected with one or more blood-borne viruses but with unknown viral load and treatment<br>Source with detectable viral load for one or more viruses<br>Source with unknown viral load but with advanced and untreated infection |
| Low risk | Infected source with completely suppressed viral load<br>Infected source with unknown viral load but under treatment and proven therapeutic adherence<br>Source with negative virologic tests at the time of the accident although but reporting the existence of risk factors for virus transmission<br>Unknown virologic status and hypothesized absence of known risk factors |
| Source with minimal risk or no risk | Recent serological tests resulted negative for viral markers and absence of recent behaviours at risk |

Note. Adapted from "HIV, Hepatitis B and Hepatitis C - Management of Health Care Workers Potentially Exposed. NSW Government. Health Procedures". Issue of May 2017. Available at website: https://www1.health.nsw.gov.au/pds/activepdsdocuments/pd2017_010.pdf (last access: 25/08/2020).

It is mandatory to consider at risk of bloodborne infections any accidental contact of mucous membranes and non-intact skin with:
- blood or any other biological material that visibly contains blood,
- body fluids, secretions, and excretions, regardless of the presence of visible traces of blood (cerebrospinal, synovial, amniotic, peritoneal, pericardial or pleural fluid, sperm, vaginal secretions) except sweat,
- organic materials (tissues, biopsy or anatomical materials, cell cultures, etc.).

On the other hand, contact with intact skin must be assessed case by case, especially if the contact occurs with biological material with highly concentration of infecting agent and if the contact affects a large skin surface.

The health activities most considered at risk of biological accident are:
- taking blood samples/phlebotomy,
- insertion or removal of devices for intravenous therapy,
- surgical interventions,
- cleaning and waste disposal operations in hospitals,
- all invasive manoeuvres, such as access to tissues, cavities, and organs in which it is necessary to overcome the skin barrier.

**Management of exposure to the risk of bloodborne virus transmission (proposed actions)**

If an HCW reports one of the following situations:

a) parenteral exposure (puncture or cut wound with sharp or cutting objects/tools contaminated with biological material),
b) mucosal exposure (splashes of biological material in the mouth or eyes),
c) contamination of intact or damaged skin (wounds, abrasions, exudative dermatitis) with biological fluids, it is mandatory

1. To immediately carry out the DECONTAMINATION:
   a) in case of a puncture wound or needlestick injury, encourage bleeding without suck the wound, wash immediately with soap and water, then disinfect the area of the exposed skin;
   b) in the event of mucosal exposure: wash the eyes with running water or physiological solution, keeping them well open, wash the face with running water and, in the case of mouth contamination: rinse the oral cavity abundantly with running water after having spat out as much material as possible along with saliva;
   c) in the event of skin contamination, whether intact or damaged: wash thoroughly with soap and water, without scrubbing, then disinfect;
   d) in case of clothes contamination: take them off immediately, take a shower if possible and wear clean clothes.
2. After decontamination, immediately REPORT the event to the Supervisor/Unit Medical Director or, in case of absence, to his/her delegate and if the accident occurs during the night or holidays, report the event to emergency medical Service, who will:
   a) carry out the appropriate counselling to help and support the exposed operator in

the procedure of filling in and signing the internal injury/biological accident report and the "Risk assessment questionnaire" (based on the information available about the "source") codified by the Quality Officer of the health facility;

b) evaluate the source of infection and any existing biological risk with information already available, if the source is known, (*e.g.* medical record, patient history, etc.) or by asking the patient source to consent to the blood sampling for the research of HBsAg, anti-HCV and anti-HIV, in order to guarantee the exposed personnel the necessary information to be able to eventually start the PEP. If the patient source does not give his/her consent, the analyses cannot be carried out and the source will be considered as an "unknown". Obviously, it is not necessary to test the patient source for HBV infection if the exposed operator has previously documented evidence of immunity for Hepatitis B (anti-HBs levels ≥10 mIU/mL or positive anti-HBc) [22];

c) notify the Preventive Medical Service Department of the incident.

3. The Department of Preventive Medical Service will finally have the task of collecting and recording all the information on the accident modalities, the source and exposed data and applying the SURVEILLANCE PROTOCOL.

**Surveillance protocol**

The surveillance protocol consists of a basal blood sampling (called "time zero") to determine and document the serological situation of the injured worker at the time of the accident. So, the exposed operator must immediately to be tested for the following tests:

- anti-HBs, HBsAg, anti-HBc (if his/her immune situation against the hepatitis B virus is not known, if he/she has not been previously vaccinated or if he/she is a "not-responder" to the vaccination);
- IV generation anti-HIV test;
- anti-HCV test.

After that, the specific follow-up must be determined by risk assessment, that is the stratification of the specific risk of infection to which the injured person is exposed (Table 4), that will depend on immunological status of both HCW and "source" (*e.g.*, if known or unknown) and after risk assessment, the PEP and the necessary laboratory tests must be established by the employer in accordance with regional, national, and European legislation and in accordance with the specific collective labour agreements.

So, according to the source, the following situations may occur:

*A. Known source (negative for HIV, HCV, and HBV)*

In the event that the source is known, negative for HIV, HBV and HCV and does not report behaviours that may have exposed him/her to risk of infection in the last 6 months, the exposed operator doesn't need to be subjected to any laboratory investigation and, if he/she has already started the PEP, it will be stopped. On the other hand, if there is a well-founded suspicion that the source has behaved at risk or if it is not possible to obtain sufficiently reliable and complete information about that, the operator will be treated as exposed to a "positive" source [22].

*B. Unknown source*

In case of unknown source or if the source is known but his/her virologic status is unknown at

**Table 4** - Follow-up of the exposed HCW based on the virological status of the "source"

| *Virological status of the "source" patient** | *Follow-up* | | |
|---|---|---|---|
| | *4 weeks* | *12 weeks* | *24 weeks* |
| HIV positive | HIV di IV gen. | HIV di IV gen. | – |
| HBV positive** | HBsAg | HBsAg | HBsAg |
| HCV positive | Anti-HCV and HCV PCR qualitative | Anti-HCV | Anti-HCV |

*If the source patient has negative serological tests after the accident, but there is a possibility that he/she is in a window period or if the source is unknown or refuses consent to the serological tests and based on the risk assessment there is a danger of infection (Tables 1-3), the healthcare worker exposed will have to follow-up as if the source were "positive".

**If the exposed worker is immune (anti-HBs ≥10 mIU/ml or anti-HBc positive), no tests for hepatitis B markers are required, regardless of the state of the source.

the time of the accident, the Unit Medical Director/Supervisor will carry out a Risk Assessment and will try to have consent from the source to be tested for HBsAg, anti-HCV and anti-HIV, in order to obtain as soon as possible the necessary information to decide if the HCW needs to start the PEP [22-23].
So, the source patient must be immediately tested for the following analysis:
– IV generation anti-HIV test
– HBsAg test (not required if the exposed HCW has shown immunity)
– anti-HCV test.
If the source is negative for HIV and/or HBV and/or HCV infection, but reports behaviours in the previous three months that possibly put him/her at risk of contracting HIV infection or at risk of contracting HBV and/or HCV in the previous six months, he/she must be warned to pay attention to any onset of signs and/or symptoms of primary infection; he/she will also be advised to repeat the virologic tests after 6, 12 and 24 weeks after the exposure to risk. In any case, until any infection in the source patient can be excluded, the exposed operator must be monitored as if he had been exposed to a "positive" source [22].
On the other hand, if the source patient does not give his/her consent to laboratory tests, the analyses cannot be carried out and he/she will be considered as an "unknown" source, therefore as a "positive" source [22].
All laboratory test results about the source must be available as soon as possible to the referring physician that, in case of positivity due to the presence of anti-HIV antibodies, will send the exposed operator to the Reference Operating Unit of Infectious Diseases to assess the onset of PEP. As already mentioned, PEP for HIV must be started within 1-4 hours from the exposure, if the elapsed time is longer but not exceeding 48 hours, in like manner the operator will start the PEP.
Obviously, it is not necessary to test the patient source for HBV infection if the exposed operator has previous documented evidence of immunity for Hepatitis B (anti-HBs levels ≥10 mIU/mL or HBcAb positive) conversely, the viral load has to be measured if the source is known to be positive or is found to be positive for HIV, HCV and/or HBV. In the latter case, if the source is not aware of his/her own positivity, he/she must be immediately referred to infectious disease counselling.

*C. Known source, HIV positive or potentially HIV positive*

In the case of a known source, HIV positive or potentially HIV positive, it is advisable to test the exposed operator immediately searching for anti-HIV antigens and antibodies using fourth generation tests, and to repeat them after 4 weeks. After that, if the tests are still negative after this period, although it is strongly suggestive of the absence of infection, the tests will be repeated also 12 weeks after the accidental event, for definitive confirmation of negativity. If the operator has been exposed to a source at high-risk of HIV infection, it would also be advisable to perform an HIV-RNA test, given that this test has the ability to detect the virus even before the production of antibodies by the infected organism. In some particularly complex cases, such as the risk of co-infection, the clinician may recommend further checks at distances greater than 12 weeks from exposure [24-28].
If there is a need to initiate HIV PEP, the exposed operator must give his/her consent before starting the drug therapy, that may take place at the reference Emergency Department or at the Infectious Diseases Department of the Structure where, before giving his/her consent, the operator will be appropriately informed about the efficacy, safety, toxicity and contraindications of the treatment and also about the consequent risks of his/her refusal. The operator must also give his/her consent to the blood sampling that, at the time "zero", must include the following tests:
1. complete blood count,
2. HBsAg, anti-HBs, anti-HBc, qualitative assay for HBV DNA (if not immunized),
3. anti-HCV, qualitative assay for HCV RNA,
4. IV generation anti-HIV assay,
5. ALT/GOT, AST/GPT, GGT, alkaline phosphatase, total bilirubin,
6. creatinine, glycemia,
7. amylase,
8. uric acid,
9. triglycerides,
10. lymphocyte subpopulations: total CD4, total CD8.

*D. Known source, HBV positive or potentially HBV positive*

Any individual found to be positive to anti-HBc test or having an anti-HBs titre ≥10mIU/mL, re-

gardless of how long it has been since vaccination, should be considered immune to hepatitis B infection by accidental event and it does not need to take any action (*e.g.*, source blood testing and PEP for HBV). In the event that, after previous vaccination, the antibody titre of the complaint is not yet known, the anti-HBs search must be carried out as soon as possible after the accident (if this is not possible, the exposed personnel must be considered as "susceptible" until there will be evidence of his/her immunity). If the exposed HCW is considered susceptible to HBV infection (anti-HBs levels <10 mIU/mL and anti-HBc negative), PEP can be strongly advised when the source is known to be HBV positive or if unknown. The PEP will consist of the administration of intramuscular hepatitis B immunoglobulin (HBIG) within 48 hours of the injury (passive immunization) and then to start vaccination (active immunization) [29]. In order to offer an efficient counselling, the source patient, if known to be positive for HBV or has been proven to be positive for HBsAg after the occupational accident, he/she must also be subjected to HBeAg and quantitative HBV DNA tests, after given consent. At this point, the exposed operator will be tested for HBsAg after 6, 12 and 24 weeks from the accident. The currently available antiviral treatments for HBV infection include two classes of therapeutic agents: pegylated interferon (PEG-IFN) and nucleoside/nucleotide analogues (NUCs). NUCs, which act through inhibition of viral polymerase, are the most commonly used and have an excellent safety profile and tolerability [30].

### Known source, HCV positive or potentially HCV positive

Although the overall risk of HCV transmission after occupational exposure is low and to date there

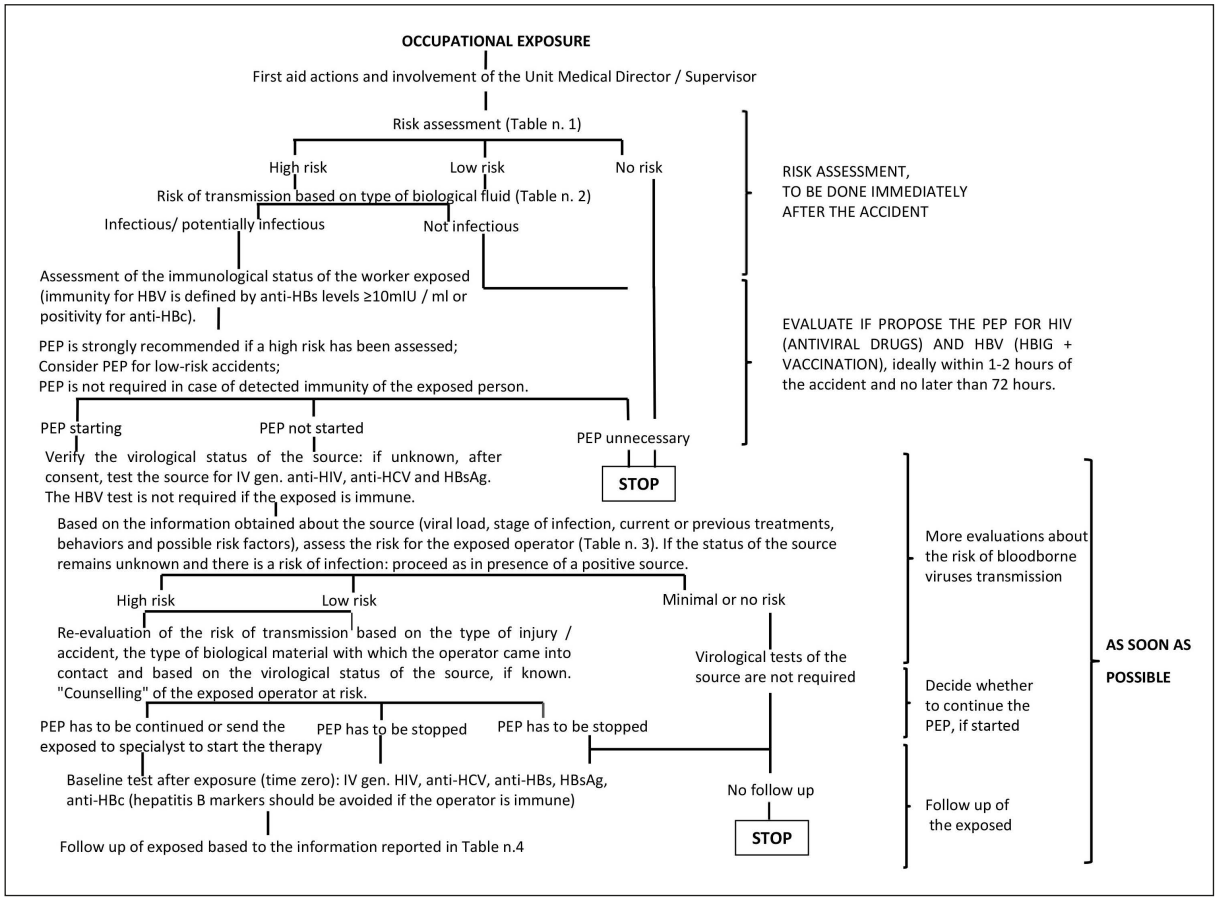


**Figure 1** - This flow-chart shows the actions to be performed in the event of an occupational accident.

is neither vaccination nor PEP that can be considered useful for HCV prevention, the therapeutic treatments currently available for the treatment of acute hepatitis C infection are highly effective. Therefore, an early identification of the infection and a sudden start of the therapy are particularly important. If the source is known to be HCV positive or is found to be positive when performing the post-exposure test for the presence of anti-HCV, the quantitative RNA of the virus must be searched, after given consent, in order to better guide the clinician in the counselling of the exposed and better assess the risk of transmission.
On the other hand, the exposed operator will be tested for qualitative HCV-RNA four weeks after the accident and for anti-HCV after 4 and 12 weeks. If the tests are still negative at week 12, the risk of infection may be considered insignificant, but further screening for HCV antibodies is usually done even 24 weeks after exposure to confirm that there has been no transmission of HCV infection [31, 32]. Although not frequent, the criterion 9 of Italian HCV guidelines describes the therapeutic opportunity with direct-acting antiviral (DAA) for infected HCW in terms of when to treat and what treatments to use [33].
This document, drawn up after a careful review of the literature data, is intended to be a simple guide to refer to in the event of an occupational biological risk accident in the healthcare environment, to be used together with the OPs codified by each healthcare facility. Particularly our document specifies the procedures to be followed and, above all, the persons in charge to refer to in the event of an occupational accident, also through some tables (Tables 1-3) and one flow-chart (Figure 1), so that action can be taken as quickly as possible in order to minimize the chances of contracting infection by the HCW involved.

**Conflicts of interest**
The authors declare no conflict of interest.

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