

# **HIV post-exposure prophylaxis**

***Guidance from the UK***

***Chief Medical Officers' Expert***

***Advisory Group on AIDS***

## DH INFORMATION READER BOX

<b>Policy</b> HR/Workforce Management Planning Clinical	Estates Performance IM & T Finance Social Care/Partnership Working
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<b>Document</b>	Best Practice Guidance
<b>Gateway Reference:</b>	10380
<b>Title</b>	HIV post-exposure prophylaxis: Guidance from the UK Chief Medical Officers' Expert Advisory Group on AIDS
<b>Author</b>	Department of Health
<b>Publication date</b>	19 September 2008
<b>Target audience</b>	PCT CEs, NHS Trust CEs, Foundation Trust CEs, Medical Directors, Directors of PH, Directors of Nursing, PCT PEC Chairs, Special HA CEs, Directors of HR, GPs, Emergency Care Leads, General Dental Practitioners, Accident and Emergency Departments, Heads of Midwifery, NHS Walk-in Centres, Consultants in Communicable Disease Control, GUM, HIV, Infectious Diseases, Virology, Microbiology, Occupational Medicine and Dental Public Health
<b>Circulation list</b>	
<b>Description</b>	Updated guidance on HIV post-exposure prophylaxis (PEP) following occupational exposure
<b>Cross reference</b>	N/A
<b>Superseded documents</b>	HIV post-exposure prophylaxis: Guidance from the UK Chief Medical Officers' Expert Advisory Group on AIDS (February 2004)
<b>Action required</b>	N/A
<b>Timing</b>	N/A
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<b>For recipient's use</b>	

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# Chapter 1: Introduction

## 1.1 Background and other sources of guidance

1. This document supersedes guidance on occupational HIV post-exposure prophylaxis (PEP) from the UK Chief Medical Officers' Expert Advisory Group on AIDS (EAGA) issued in February 2004 (1) and the interim update following the withdrawal of Viracept (nelfinavir) published in July 2007 (2). It should be read in conjunction with local needlestick injury policy.
2. The following sections have been clarified after reviewing the available evidence:
  - Maximum recommended interval between exposure and commencing PEP (paragraph 45).
  - Revised recommended schedule of serological investigations following occupational exposure to HIV, based on evidence from national surveillance of significant occupational exposures to blood-borne viruses, expert opinion and practicalities of application (Box 1, pages 21–23).
  - Recommended regimen for PEP starter packs (Annex C, paragraph 5).
3. Other significant amendments include:
  - Clarifying the implications of the Human Tissue Act 2004 and the Mental Capacity Act 2005 for testing incapacitated source (adult) patients for serious communicable diseases without consent (paragraph 32). and associated changes to Annex B.
  - A recommendation for good practice that all hospitals have the capacity to obtain an HIV test result (for source patient testing) ideally within 8 hours and not more than 24 hours after blood is taken (paragraph 34).

- The section on exposure outside the hospital setting has been shortened (Chapter 5). It cross-references guidance on PEP following sexual (non-occupational) exposure from the British Association for Sexual Health and HIV (BASHH) (3), which EAGA endorses. The BASHH guidance was reinforced by the Chief Medical Officer in a letter recommending PEP for sexual (non-occupational) exposure be made available as part of sexual health services in England (4).
  - Addition of a new Annex H summarising the evidence from animal and clinical studies on the maximum interval between exposure and commencing PEP.
4. Those responsible for occupational health provision to people in professions where there may be a risk of exposure to HIV-infected material outside health care settings (e.g. police, prison and fire service, voluntary aid agencies, armed forces) may wish to use these guidelines as a basis for developing guidance relevant to their own occupational setting. For example, advice to the Scottish Executive on guidance needed to protect front-line workers and victims of crime from blood-borne viral infections (5) refers to EAGA's guidance.
  5. Related guidance from the Advisory Committee on Dangerous Pathogens on *Protection against blood-borne infections in the workplace: HIV and hepatitis* (6) is currently undergoing revision. NHS Employers has issued the *Healthy workplaces handbook* (7) (<http://www.nhsemployers.org/practice/practice-2912.cfm>), which has replaced the *Blue Book (The management of health, safety and welfare issues for NHS staff)*.
  6. This document offers guidance on:
    - assessing the risk to a health care worker of acquiring HIV infection following occupational exposure;
    - when to recommend PEP;

- the choice of drugs;
- how to ensure that all health care workers have **immediate, 24-hour access** to advice on PEP, to drugs and to appropriate support;
- devising local PEP policies and protocols;
- appropriate support arrangements for health care workers seconded overseas, including medical students on 'electives';
- provision of PEP for exposures to HIV occurring outside the hospital setting;
- antiretroviral drug resistance;
- laboratory workers who may be exposed to unusual and/or highly resistant viruses;
- considerations about PEP for exposed women who are, or may be, pregnant;
- drug interactions; and
- PEP for patients after possible exposure to an infected health care worker.

## 1.2 General principles

7. In reviewing the guidance, EAGA's PEP Working Group (see Annex I) highlighted the following basic principles, which apply to the management of all exposures to HIV (i.e. occupational and non-occupational):
  - EAGA recommends the inclusion of local PEP policy guidance in induction programmes for new staff to educate and raise awareness among those at risk, including where to access PEP and the need for prompt attendance.
  - Timely provision of PEP (24-hour access).
  - Risk assessment.
  - Management and follow-up of all exposed individuals.



8. Occupational exposure to blood and body fluids potentially infected with HIV and other blood-borne viruses is unnecessarily common. Many exposures result from a failure to follow recommended procedures, including the safe handling and disposal of needles and syringes, or wearing personal protective eyewear where indicated.
9. Prevention of avoidable exposure is of prime importance. Adherence to the *Code of Practice for the Prevention and Control of Healthcare Associated Infections* (8), made under the Health Act 2006, which includes prevention of blood-borne virus infection, will serve to reduce the incidence of occupational exposures to a minimum.
10. This document concerns exposure to HIV and post-exposure prophylaxis. Any significant exposure to blood and some other body fluids or tissues (see Annex A) has the potential to transmit other blood-borne virus infections, such as hepatitis B (HBV) and hepatitis C (HCV). Therefore, an integrated approach to post-exposure management with respect to HIV, HBV and HCV is recommended.
11. There will remain occasions when exposure occurs despite careful attention to the correct procedures. If, despite measures being in place, exposure has occurred, it is a requirement under the Control of Substances Hazardous to Health (COSHH) Regulations 2002 to review the risk assessment (Reg 6(3)).
12. All health care workers in hospital and elsewhere (e.g. general medical and dental practitioners, community health care workers) should be informed and educated about the possible risks from occupational exposure and should be aware of the importance of seeking urgent advice following any needlestick injury or other occupational exposure (see paragraph 24). Training should ensure that everyone knows to whom to report (COSHH Reg 12). The guidance applies equally to students in health care settings.

13. Every NHS employer should have a policy on the management of exposures, which should specify the local arrangements for risk assessment, advice and the provision of PEP (8). This policy must ensure that adequate 24-hour cover is available and should designate one or more doctors who exposed persons may be referred to urgently for advice. Primary responsibility should lie with the occupational health service, with out-of-hours cover provided by Accident and Emergency (A&E) departments, unless there are other arrangements locally for out-of-hours cover to be provided by, for example, occupational health services. A&E departments would be expected to have access to on-call expert advice. Sources of such advice may include consultants in occupational health, HIV disease, genito-urinary medicine, virology, microbiology, infectious diseases and public health medicine. There should be clear channels for access to any necessary expert advice about HIV and PEP drugs.

### 1.3 HIV and significant occupational exposure

14. The risk of acquiring HIV infection following occupational exposure to HIV-infected blood is **low**. Epidemiological studies have indicated that the average risk for HIV transmission after percutaneous exposure to HIV-infected blood in health care settings is about 3 per 1,000 injuries. After a mucocutaneous exposure, the average risk is estimated at less than 1 in 1,000. It has been considered that there is no risk of HIV transmission where intact skin is exposed to HIV-infected blood.
15. A case–control study conducted by the US Centers for Disease Control and Prevention concluded that the administration of zidovudine prophylaxis to health care workers occupationally exposed to HIV was associated with an 81% reduction in the risk for occupationally acquired HIV infection (9). Four factors were associated with increased risk of occupationally acquired HIV infection:

- Deep injury.
  - Visible blood on the device which caused the injury.
  - Injury with a needle which had been placed in a source patient's artery or vein.
  - Terminal HIV-related illness in the source patient.<sup>1</sup>
16. It was estimated that the risk for HIV transmission after percutaneous exposures involving larger volumes of blood (i.e. where there was visible blood on the needle or in the syringe), particularly if the source patient's viral load was likely to be high, exceeds the average risk of 3 per 1,000.
  17. Information about primary HIV infection and evidence from animal models indicate that systemic viral dissemination does not occur immediately, leaving a window of opportunity during which post-exposure antiretroviral medication may be beneficial.
  18. In established HIV infection, combinations of antiretroviral drugs are more potent than zidovudine alone in suppressing viral replication. This, together with the rise in prevalence of antiretroviral drug resistance amongst HIV-infected individuals (10; 11), has led to the introduction of combination antiretroviral drug prophylaxis following occupational exposure to HIV.
  19. EAGA has considered the evidence for the efficacy of PEP with antiretroviral drugs and recommends that their use should be considered in certain circumstances. Other sources of information include reviews of antiretroviral PEP post-occupational exposure to HIV (12; 13), US guidelines (14) and their application in clinical practice (15), and consensus European guidelines (16).

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<sup>1</sup> Where the source patient is not on therapy and has uncontrolled viral load.

## 1.4 Surveillance of occupational PEP usage

20. The Health Protection Agency (HPA) has undertaken enhanced surveillance of significant occupational (percutaneous and mucocutaneous) exposure to blood-borne viruses (BBVs) in health care workers since 1997 (17). Around 200 centres in England, Wales and Northern Ireland participate (not full national coverage). Reporting is voluntary and only incidents involving exposure to a BBV-positive source, or where HIV PEP is initiated, are included. This provides current as well as historical data on PEP usage and HIV exposures. Initial reports from participating centres (mainly Occupational Health departments but also Genito-Urinary Medicine (GUM), Virology and Microbiology departments) are followed up at 6 weeks and 24 weeks and provide further information on the incident, testing of the source, what PEP was prescribed, reasons for discontinuation etc. Findings from this surveillance have informed revisions to the guidance.
21. Some of the key findings relating to occupational exposure to HIV, as reported to the scheme by October 2007, for incidents occurring in 2005–06 (HPA, unpublished data) are:
- Of the initial reports, 50% (482/956) involved exposures to hepatitis C and 25% (238/956) exposures to HIV. Overall, 29% (276/956) of reports involved HIV exposures, including to co-infected source patients.
  - Of those exposed to an HIV-positive source (including exposures to co-infected source patients), 57% (157/276) of health care workers commenced PEP following a percutaneous exposure and 24% (66/276) following mucocutaneous exposure. 18% (51/276) did not take PEP and for the remainder the PEP status was unknown (<1% (2/276)).
  - Where a time to commencing PEP was reported on the 6-week follow-up form, 38% (62/163) started PEP within an hour of exposure and 90% (147/163) overall

within 24 hours. Only 3% (5/163) were reported to have started PEP over 72 hours post-exposure.

- Where length of time on PEP was stated on the 6-week follow-up form, 17% (23/132) of health care workers exposed to an HIV-positive source discontinued all or part of their PEP regimen prematurely because of drug toxicity and 44% (8/18) of those exposed to a source of unknown status completed the 28-day course of PEP.
- In cases where PEP was initiated but the source was found to be negative, 52% (44/85) of health care workers had discontinued PEP within a day of initiating treatment, and 86% (73/85) overall had stopped within 7 days or fewer.
- Of 276 HIV-exposed health care workers originally reported to the scheme, 58% (161/276) were reported (on the 24-week follow-up form) to have undergone HIV post-exposure testing, with 46% (127/276) completing the recommended 24 weeks of follow-up.
- Five cases of HIV seroconversion in UK health care workers have been documented; four occurred in or before 1993, only one of whom received PEP (zidovudine monotherapy). The most recent case was in 1999, when seroconversion occurred despite combination PEP (18).

22. Locally conducted audits of occupational exposure to HIV and use of PEP have been reported (19; 20).

## Chapter 2: Risk assessment

### 2.1 Immediate action

23. Immediately following **any** exposure – whether or not the source is known to pose a risk of infection – the site of exposure, e.g. wound or non-intact skin, should be washed liberally with soap and water but without scrubbing. Antiseptics and skin washes should not be used – there is no evidence of their efficacy, and their effect on local defences is unknown. Free bleeding of puncture wounds should be encouraged gently but wounds should not be sucked. Exposed mucous membranes, including conjunctivae, should be irrigated copiously with water, before and after removing any contact lenses.
24. Prompt reporting of injuries is a necessary first step to enabling appropriate and rapid prescribing of PEP. A risk assessment needs to be made urgently by someone other than the exposed worker about the appropriateness of starting PEP, ideally an appropriately trained doctor designated according to local arrangements for the provision of urgent post-exposure advice. This guidance refers only to the issue of HIV post-exposure prophylaxis. Consideration should also be given to risk of exposure to hepatitis B and hepatitis C. An integrated approach to post-exposure management is provided in guidance from EAGA and the Advisory Group on Hepatitis (AGH) (21).

### 2.2 Circumstances of exposure

25. The issue of PEP should be considered after an exposure with the potential to transmit HIV, based on the type of body fluid or substance involved, and the route and severity of the exposure.
26. The designated doctor or other practitioner should first assess if the exposure reported by the health care worker

was **significant** – that is, with the potential to transmit HIV. There are three types of exposure in health care settings associated with significant risk. These are:

- (i) percutaneous injury (from needles, instruments, bone fragments, significant bites which break the skin etc);
- (ii) exposure of broken skin (abrasions, cuts, eczema etc);  
and
- (iii) exposure of mucous membranes including the eye.

(Note – the history and examination may highlight the need to institute other prophylactic and investigative regimens, e.g. antibiotic therapy, hepatitis B immunisation).

27. Some health care workers may have had occupational exposures which, after careful assessment, are not considered significant – i.e. they do not have the potential for HIV transmission. Such workers should be advised that the potential side effects and toxicity of taking PEP outweigh the negligible risk of transmission posed by the **type of exposure** because it is considered insignificant, whether or not the source patient is known or considered likely to be HIV infected.

### 2.3 Assessment and testing of the source patient

28. If initial assessment indicates that an exposure has been **significant** – that is, with the potential for HIV transmission – consideration should then be given to the HIV status of the source patient. It may be possible to ascertain from the medical record that a source patient has established HIV infection. Results from animal studies suggest that HIV PEP is most likely to be efficacious if started within the hour. An urgent preliminary risk assessment therefore should assess if it is appropriate to recommend taking the first dose of PEP. A more thorough risk assessment should be undertaken to inform a decision about whether to continue the regimen (see also paragraphs 39 and 40).

29. The designated doctor should ensure that appropriate arrangements are made to approach a source patient whose HIV status is not known and ask for their informed agreement to HIV testing. **This approach should not be undertaken by the exposed worker**, but may be made by another member of the clinical team responsible for the patient, subject to local arrangements. A universal approach to asking source patients to agree to have an HIV test avoids the need to make difficult judgements, simplifies and normalises the process and avoids potential discrimination against people perceived as belonging to groups associated with higher than average HIV prevalence.
30. When a source patient is asked to agree to undergo HIV testing, careful pre-test discussion will be needed, as will informed consent, which should include disclosure of the source patient's test result to the occupational health service and to the health care worker. This pre-test discussion can be provided by any appropriately trained and competent health care worker. Specialist pre-test discussion may sometimes be considered appropriate if the circumstances of the source patient are unusual or complex (e.g. source patient does not speak English, has mental health problems or a learning disability). For guidance on HIV testing, see references 22 and 23.
31. It is not considered acceptable to seek consent for source patient testing before surgery to guard against an exposure incident occurring during the procedure. Consent for testing should only be sought from the source patient after the exposure incident has occurred and its significance has been assessed. If there are practical obstacles to obtaining consent promptly (e.g. the patient is still under the influence of a general anaesthetic or has been discharged home), the decision to initiate PEP should be based on the available information. Ideally, patients at high risk of being infected with a blood-borne virus should be identified pre-operatively and offered testing on clinical grounds at that stage. This is



consistent with best practice for improving the detection and diagnosis of HIV in non-HIV specialties advocated by the Chief Medical Officer (24).

32. Section 1(1)(f) of the Human Tissue Act 2004 allows “relevant material” (which is defined as anything containing cells and would therefore include tissue, whole blood and other body fluids) to be used to obtain scientific or medical information about a person which may affect another person “if done with appropriate consent”. This means that where a source patient lacks capacity to consent (e.g. because they are unconscious), his/her tissue etc can only lawfully be tested for serious communicable diseases if it is reasonably held to be in his/her best interests in accordance with the Mental Capacity Act 2005. In the light of this, the General Medical Council withdrew its guidance that set out exceptional circumstances in which the testing of an existing sample might be justifiable (see Annex B). In the event of a deceased patient being the source of a needlestick injury and whose HIV status is unknown, the taking and testing of samples requires consent in accordance with the Human Tissue Act 2004. Assuming the deceased did not give consent (or refuse it) while alive, this can be obtained from a “nominated representative” (if appointed) or by a person in a “qualifying relationship” to the deceased.
33. As part of pre-test discussion, or before asking about a history of possible exposure to HIV, the source patient should first be informed about the incident and the reason for the enquiry, request for a test and to whom the results will be disclosed. The difficulties of the exposed health care worker’s situation should be discussed – either in terms of the worker not missing the opportunity to benefit from PEP, or conversely not being subjected unnecessarily to its potentially unpleasant short-term and unknown long-term side effects. Wherever possible, the health care worker’s identity should not be disclosed. It is understood

that consent to HIV testing is rarely withheld in these circumstances, when the approach is made in a sensitive manner.

34. Testing of source patients' blood should be conducted urgently. This is to minimise exposure to antiretroviral medication and to allay anxiety of the exposed individual. **It is recommended good practice that all hospitals have the capacity to obtain an HIV test result ideally within 8 hours and not more than 24 hours after source blood is taken.** Starting PEP, where appropriate, should not be delayed to await the result of source patient testing. The use of a rapid (near-patient) HIV test can reduce the time needed to rule out HIV infection to a few hours or less, and may be useful where obtaining a laboratory test result will be delayed. A negative result with a highly sensitive rapid test is reliable evidence that infection is not present. A positive test is presumptive evidence of HIV infection, but confirmatory tests should be performed.
35. Any source patient who is newly diagnosed HIV positive as a result of this process will need immediate access to specialist post-test counselling and assurances about confidentiality. Close support and clinical management will be needed on an ongoing basis. Source patients should also be informed promptly of HIV negative results, with any post-test discussion appropriate to individual circumstances (e.g. to address an ongoing risk identified through pre-test discussion and as a reminder about the window period if there has been recent personal risk). The possibility of a window period infection in the source patient should be addressed as part of the risk assessment, and PEP for the exposed worker may be recommended.

#### 2.4 Exposure to discarded needle/unknown source

36. Where it is not possible to identify the source patient (e.g. needlestick injury caused by a discarded needle), a risk

assessment should be conducted to determine whether the exposure was significant. This will be informed by considering the circumstances of the exposure and the epidemiological likelihood of HIV in the source. The use of PEP is unlikely to be justified in the majority of such exposures (25).

# Chapter 3: PEP

## 3.1 When to prescribe PEP

37. PEP should be recommended to health care workers if they have had a significant occupational exposure (see paragraph 26) to blood or another high-risk body fluid (see Annex A) from a patient or other source either known to be HIV infected, or considered to be at high risk of HIV infection, but where the result of an HIV test has not or cannot be obtained, for whatever reason.
38. PEP should not be offered after exposure through any route with low-risk materials (e.g. urine, vomit, saliva, faeces) unless they are visibly bloodstained (e.g. saliva in association with dentistry). Also, PEP should not be offered where testing has shown that the source is HIV negative, or if risk assessment has concluded that HIV infection of the source is highly unlikely. Exceptionally, PEP may be indicated following a negative test if there is reason to suspect the source may be seroconverting (i.e. in the window period).
39. When offering PEP it is important to take into account any views of the exposed health care worker. Depending on the outcome of the preliminary risk assessment, if the exposure was significant, the exposed health care worker may wish to consider starting PEP until further information is available about the source patient. In this way the option of possible benefit from prompt PEP will have been kept open. Changes can be made to the PEP regimen, including cessation, if further information becomes available.
40. If the HIV status of the source cannot be established, the exposed health care worker should have the opportunity to consider whether or not to continue PEP. Their decision should be informed by all that is known about the source patient in terms of past exposure to risk of HIV infection and also the nature and severity of the exposure. These

aspects should be considered together with the potential for unpleasant short-term adverse effects and unknown long-term effects of taking PEP drugs.

41. The relative risk of transmission may be increased considerably if the source patient has a high plasma viral load (e.g. at the time of seroconversion or in the later stages of HIV disease). It must be appreciated that the absolute risk is difficult to determine from plasma viral load alone due, for example, to differences in viral load between body compartments (e.g. plasma and genital tract, which is relevant to sexual transmission). Nevertheless, infectivity of all body fluids is likely to be reduced where plasma viral load is undetectable (26; 27).
42. The use of PEP drugs in special circumstances (e.g. pregnancy), the place of alternative drug regimens and viral drug resistance are discussed in Annex E. Drug interactions are considered in Annex F.

### **3.2 What to prescribe for PEP**

43. Annex C describes the currently recommended PEP starter regimen and the rationale for its choice. PEP is not a licensed indication for any of the antiretroviral drugs, which are therefore prescribed on an 'off-label' basis in the context of PEP. It is important that the ready accessibility of PEP starter packs does not conflict with appropriate prescribing practice.

### **3.3 Management of health care workers occupationally exposed to HIV: further issues, including follow-up**

44. Occupational exposure to known or suspected HIV-infected materials is always stressful and, for some, extremely so (28).
45. PEP is most likely to be effective when initiated as soon as possible (within hours, and certainly within 48–72 hours of exposure), and continued for at least 28 days. It should be noted that the evidence base on which these conclusions are based is limited (see Annex H for a summary of the

evidence). Therefore, PEP should be commenced as soon as possible after exposure, allowing for careful risk assessment, ideally within an hour. PEP is generally not recommended beyond 72 hours post-exposure. Decisions on initiation of PEP more than 72 hours after the exposure should be left to the discretion of local clinicians in discussion with the exposure recipient, in full knowledge of the lack of evidence of efficacy after this time point.

46. Following exposures for which PEP is considered appropriate, health care workers should be given time to discuss the balance of risks in their particular situation and they should be offered appropriate psychological support. They should be informed that knowledge about the efficacy and toxicity of drugs used for PEP is limited. It is important that their views about PEP are taken into account and that their preferences about what to discuss and with whom are respected. In particular, there may be someone in whom they have trust and to whom they would like to be referred.
47. The evaluation of the health care worker should cover medical history, including sexual history. Details of any existing medication should be established, as antiretroviral medications may have potentially serious interactions with other prescription or non-prescription drugs (see Annex F). Females should be asked specifically about the possibility of pregnancy (see Annex E). All exposed health care workers should be encouraged to provide a baseline blood sample for storage and a follow-up sample for testing (see Box 1, pages 21–23). The practice of taking a 6-month sample for storage only is inappropriate. It is sufficient to retain baseline samples for 2 years. The health care worker should be informed of the retention policy at the time the sample is taken.
48. All information about the health care worker and the source patient should be kept confidential. The designated doctor, who co-ordinates arrangements for source patient testing

and follow-up of the health care worker, is responsible for ensuring that issues relating to confidentiality are addressed.

49. PEP should normally be continued for 4 weeks. Every effort should be made to facilitate adherence to a full 4-week regimen. This time course, or the drugs used, may need to be modified if problems of tolerance and/or toxicity are encountered (see also Annex C). Since nausea is a common problem, the prescription of prophylactic anti-emetics should be considered. If severe nausea is experienced and is a deterrent to taking PEP, expert advice should be sought. Anti-motility drugs may be helpful if diarrhoea develops – a common side effect of protease inhibitor therapy.
50. Occupational health practitioners may choose to refer exposed health care workers to HIV, GUM or infectious disease departments for regular medical follow-up during the period of PEP, to monitor possible toxicity and adherence to the antiretroviral regimen. Close follow-up and encouragement, ideally on a weekly basis at least, from a clinician experienced in prescribing antiretroviral therapy is likely to help improve adherence and deal promptly with concerns and complications. Any need for sickness absence associated with adverse effects of PEP drugs following an occupational exposure should preferably not contribute to an individual's sickness absence record (for monitoring and absence control purposes).
51. All health care workers occupationally exposed to HIV should have follow-up counselling, post-exposure testing and medical evaluation **whether or not** they have received PEP. In addition, they should be encouraged to seek medical advice about any acute illness that occurs during the follow-up period. Illnesses characterised by fever, rash, myalgia, fatigue, malaise or lymphadenopathy may represent a seroconversion illness. Some of these symptoms may, however, be side effects of antiretroviral medication (see also Annex C).

52. It is recommended that, where health care worker follow-up is conducted outside the Occupational Health department, for example by the GUM or Infectious Diseases (ID) department, the health care worker also arranges a meeting/updates occupational health or gives consent for GUM/ID to provide the follow-up information to occupational health. This will ensure that records are complete for local review of PEP practice (see paragraph 79) and for reporting to surveillance systems (Annex D), e.g. what drugs were prescribed, tolerability of the regimen, side effects, premature discontinuation and results of any post-exposure testing.

### **Box 1: Recommended schedule of serological investigations following occupational exposure to HIV**

Until now, EAGA has recommended that follow-up testing of health care workers be performed at 12 and 24 weeks post-exposure (or 24 weeks after cessation of PEP if prescribed), using the most sensitive tests (i.e. fourth generation combined antibody/antigen assays). A baseline sample should be taken for storage. Serological testing at 6 weeks is not routinely warranted as a negative serology result at this stage is inconclusive.

Implementation of this follow-up schedule has been monitored through the national surveillance of occupational exposure to blood-borne viruses in health care workers operated by the Health Protection Agency (see Annex D) (17). Of 276 health care workers exposed to an HIV-positive source in 2005–06, fewer than half (46% (126/276)) are known to have completed 24-week follow-up (17).



There has been only a single case of HIV seroconversion in the UK where the health care worker took PEP (18) and no cases of delayed seroconversion (i.e. beyond 12 weeks from exposure) have been reported from international collaborators since the widespread use of PEP (29).

Data on the optimal duration of follow-up are limited. However, based on expert opinion, EAGA now recommends, **as a minimum, that follow-up should be for at least 12 weeks after the HIV exposure event or, if PEP was taken, for at least 12 weeks from when PEP was stopped.**

There are a number of practical arguments in favour of terminating follow-up with serological testing a minimum of 12 weeks after the exposure incident/cessation of PEP. The principal reasons are:

- a negative test at 12 weeks provides a very high level of confidence of freedom from infection (due to high sensitivity of combined antibody/antigen serological assays);
- to minimise the period of anxiety suffered by exposed health care workers waiting for the 'all clear';
- to focus efforts and resources of Occupational Health departments on improving completeness of 12-week follow-up testing;
- in the majority of cases where seroconversion has occurred following occupational exposure despite the use of triple PEP, seroconversion has been detected within 12 weeks of exposure (29); and
- for consistency with the advice following a potential sexual exposure (presenting too late for consideration of PEP), where a negative test at 12 weeks post-exposure provides reassurance of freedom from infection.

Longer follow-up with additional testing may be indicated in complex cases, for example if the exposed worker is immunocompromised, experiences an illness compatible with an acute retroviral syndrome (regardless of the interval since exposure) or where the source patient is dually infected. In the case of HIV and hepatitis C co-infection, delayed seroconversion for HIV (documented at 7 months post sexual exposure) has been reported (30). Testing for the other blood-borne viruses should follow recommended schedules.

Plasma RNA polymerase chain reaction (PCR) testing has no role to play in routine follow-up of occupational exposures to HIV. Since these tests are optimised to measure very low levels of HIV RNA, they have a relatively high rate of false-positive results and a low positive predictive value when used to detect occupational transmission.

53. Pending follow-up, and in the absence of seroconversion, health care workers who have been exposed to HIV occupationally need not be subject to any modification of their working practices, for example avoidance of exposure-prone procedures.<sup>2</sup> Advice should, however, be given to reinforce the importance of infection control measures, safer sex and avoiding blood donation during the follow-up period. This position reflects a judgement that the risk to the health care worker of becoming infected may both be high enough to justify taking PEP and engaging in safer sex but remote enough not to warrant modification of work

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<sup>2</sup> Exposure-prone procedures are those where there is a risk that injury to the health care worker may result in exposure of the patient's open tissues to the blood of the health care worker. These procedures include those where the worker's gloved hands may be in contact with sharp instruments, needle tips or sharp tissues (spicules of bone or teeth) inside a patient's open body cavity, wound or confined anatomical space, where the hands or fingertips may not be completely visible at all times. An illustrative list of exposure-prone procedures can be found in reference 31.

activities (because the risk to the patient is the product of the low risk of the health care worker becoming infected multiplied by the low risk of onward transmission to the patient through exposure-prone procedures).

54. If a health care worker presents having recently been exposed to HIV **non-occupationally**, a risk assessment should be conducted of the actual exposure. PEP may be indicated if the worker presents within 72 hours of the exposure event (3). The risk of seroconversion may be substantially higher from a non-occupational exposure. Where the exposure, or most recent in a series of exposures, is within the last 3 months, the worker may be in the window period for seroconversion. If he/she performs exposure-prone procedures, modifying their practice during the follow-up period needs to be considered.

### 3.4 HIV seroconversion

55. If, during the follow-up period, HIV infection is diagnosed, the health care worker should be advised and managed in line with EAGA recommendations (31). Health care workers who have acquired HIV infection because of exposure to HIV-infected material in the workplace, e.g. a significant occupational exposure such as a needlestick injury, may be eligible for benefits.
56. The NHS Injury Benefits Scheme (or HPSS Injury Benefits Scheme in Northern Ireland) is part of the terms and conditions of service for NHS employees. It provides temporary or permanent benefits for all NHS employees who are either on leave of absence (usually certified sick leave) and lose pay, or who have to leave their NHS job and suffer a permanent reduction in their earning ability of more than 10%, because of an injury or disease that is wholly or mainly attributable to the duties of their NHS employment.
57. The scheme is available also to general medical and dental practitioners working in the NHS. Under the terms of the

scheme it must be established whether, on the balance of probabilities, the injury or disease was acquired during the course of NHS work. Further useful information is available from: <http://www.injurybenefit.nhsbsa.nhs.uk/>

58. At least 12 weeks should elapse after cessation of PEP before a negative serology test is used to reassure the individual that infection has not occurred. Following any occupational exposure to HIV, whether or not PEP was prescribed, health care workers should attend for occupational health follow-up for such a period, and be prepared to report symptoms of concern at any time.

### 3.5 Making PEP available: immediate access

59. It is recommended that, for optimal efficacy, **PEP should be commenced as soon as possible after exposure, allowing for careful risk assessment, ideally within an hour. PEP is generally not recommended beyond 72 hours post-exposure.** There may be circumstances where it is appropriate that the exposed worker is offered the initial doses immediately, pending fuller discussion and risk assessment as soon as practicable.
60. Starter packs of the recommended drugs should be kept in a number of readily accessible and well advertised places, including:
  - Occupational Health department;
  - Pharmacy;
  - A&E department; and
  - specific wards or departments.
61. Each pack should contain a minimum 3-day course of the drugs, sufficient to cover weekends and bank holidays, with two packs to be given to cover longer bank holiday weekends.

62. Arrangements will need to be in place to ensure that starter packs are stored appropriately and that the drugs have not passed their expiry date.
63. Training and clear protocols should be given to personnel who might be responsible for initial administration of drugs.

### 3.6 Making PEP available: policies and protocols

64. Consultants in Communicable Disease Control or, in Scotland, Consultants in Public Health Medicine (CD & EH) should help ensure that the management of NHS bodies and other health care settings (including private facilities) is aware of its responsibility to make adequate arrangements for staff (8). This would include ensuring that A&E departments are aware of, and have accepted, their responsibility to provide cover, where applicable. As part of the commissioning process, these arrangements should be audited.
65. NHS bodies have a duty to adhere to policies and protocols applicable to infection prevention and control, including the prevention of occupational exposure to blood-borne viruses (8). Where appropriate, standard PEP starter packs should be available on site for use following occupational exposure. In those settings where PEP is not available on site, the policy and protocol should include information about where the starter pack of drugs may be obtained.
66. Managers should ensure that PEP policies and protocols reflect current best practice.
67. To minimise delay in seeking advice about PEP, it is important that all health care workers are aware of the possible risks from occupational exposure and the need to seek urgent advice following any percutaneous or other potentially significant exposure. All should be aware of how to report an exposure, and to whom. Occupational Health departments should issue regular reminders to all those for whom it is responsible, including non-hospital health

care workers who have contracted cover for post-exposure management (e.g. general medical and dental practitioners and their staff).

68. Local factors will vary between trusts and other health care settings and first-line provision of PEP will depend on these.
69. Sources of expert advice should be indicated in local policies and may include:
  - Consultants working in HIV medicine, Virology, Microbiology, Infectious Diseases, GUM, Occupational Health; and
  - Public Health Physicians (particularly those with responsibility for infection control such as Consultants in Communicable Disease Control or, in Scotland, Consultants in Public Health Medicine (CD & EH)).
70. In trusts where there is a consultant occupational physician in post, it is likely that arrangements will be co-ordinated through the Occupational Health department. Where there is no consultant occupational physician, hospitals may group together on a geographical basis for advice through a central consultant occupational physician.
71. Where there is no consultant occupational physician, the policy should specify who is responsible for provision of PEP and its follow-up according to local expertise and logistics.
72. In view of the need for very prompt treatment and the serious consequences of HIV seroconversion, significant occupational exposure to known or possible sources of HIV constitutes a medical emergency. Outside normal working hours, A&E departments would usually be expected to assume responsibility for assessment of occupational exposure and providing PEP. As the first point of contact for any such exposure, whether or not this arose in the hospital, there is a need to give appropriate priority to potential PEP candidates. A&E staff, such as junior medical staff and triage nurses, will require specific training regarding assessment

of the need to access immediate expert advice and about supplying an initial dose of PEP, and clear protocols to follow. As key 'stakeholders', it is important that A&E departmental staff are involved in developing and agreeing local PEP policies and protocols.

73. In other health care settings, it will be important for general medical and dental practitioners, their staff and other community health workers to ensure they have arrangements in place for rapid access to urgent advice, and PEP where indicated. This will be particularly important for GPs and networks of carers who know they are looking after one or more HIV-infected patients – for instance, in the context of terminal illness. If friends or relatives are providing clinical care to HIV-infected patients in the community which involves a risk of exposure to HIV-infected material, they should be advised about infection control measures to prevent exposure (21; 32), and the importance of reporting any exposure incidents to the A&E department without delay.
74. Those responsible for occupational health and safety of certain non-health care workers (such as police, fire and prison service personnel), who may also be at risk of occupational exposure to HIV, should ensure that there are similar arrangements in place for access to advice in such an emergency and assessment and treatment where appropriate.
75. Back-up information for community health care workers via a widely publicised local helpline may be helpful, as well as locally disseminated guidelines on appropriate local sources of expert advice as in paragraph 69 above.
76. It would normally be appropriate for the starter packs of PEP drugs to be made available to community-based health workers through A&E departments on a 24-hour basis.

77. It is suggested that local PEP policies should include the following information:

- occupational risks of HIV for health care workers;
- definition of “significant occupational exposure” (see paragraphs 26 and 27);
- clear protocols for post-exposure assessment, management and prescription of PEP drugs;
- rationale for therapy offered;
- sources of emergency advice and sources of subsequent support for the psychological consequences of the incident;
- out-of-hours access (e.g. when the Occupational Health department is closed);
- procedures following an occupational exposure;
- timing and duration of PEP;
- sites of starter packs;
- possible side effects of drugs and possible interactions with other medication (including ‘over the counter’ preparations);
- ensuring that local sources of expertise have access to appropriate training to maintain up-to-date knowledge of issues surrounding PEP, and to sources of expert advice for consultation where indicated, such as physicians experienced in the treatment of HIV and familiar with considerations for the use of PEP;
- arrangements for follow-up visits, follow-up testing, record keeping and confidentiality;
- voluntary reporting of occupational exposures to the Health Protection Agency’s Centre for Infections or Health Protection Scotland (see Annex D, paragraphs 1 and 2). Specific types of accident, and development of HIV disease as a consequence of occupational exposure,



require reporting under the Reporting of Injuries, Diseases and Dangerous Occurrences (RIDDOR) legislation (see Annex D, paragraphs 4–6); and

- local procedures for reporting accidents and keeping lists of laboratory employees intentionally working with Hazard Group 3 pathogens (COSHH schedule 3).

78. **Staff training** issues include:

- avoidance of occupational exposure to HIV by adherence to safer working practices and use of personal protective equipment as appropriate (8);
- action to be taken following possible exposure including immediate first aid. Clear information should be provided to all health care workers about where emergency advice and assessment can be obtained;
- the importance of reporting all percutaneous and other potentially significant occupational exposures according to local arrangements;
- encouraging health care workers particularly at risk to maintain awareness of the principles of PEP. Some may wish to consider the pros and cons of PEP before any event, although views may change depending on the particular circumstances of an exposure; and
- training of junior staff (e.g. triage nurses and junior doctors in A&E departments) who may be called upon to assist a colleague immediately after an incident and who may be responsible for supplying a starter pack. Detailed and clear protocols should be available.

79. The Occupational Health department (or other designated department for reporting blood exposures) should keep a database of exposure incidents. It is very important that all exposure incidents are reviewed, whether or not PEP was prescribed:

- to consider how recurrence might be prevented; and
  - to inform staff training as appropriate.
80. Responsibility for review should be made clear. It may vary according to local arrangements for provision of occupational health services and management of exposure incidents. Hospital or Community Infection Control Teams should be involved.

## Chapter 4: UK health care workers seconded overseas including students on electives

81. Antiretroviral medication has become more widely available in high HIV prevalence countries. Prior to departure, enquiries should be made as to whether PEP protocols are established in the centres where UK health care workers will be based. Only if PEP is not available, or it has not been possible to establish in advance whether it is available, should they consider taking a PEP starter pack with them (see paragraph 90).
82. There are occasions when health care workers may leave the UK to work abroad, some of whom intend to return to work in the UK in the future. Included in such a group are those UK medical, dental and nursing students who travel abroad during an 'elective' period to gain experience, often in developing countries. On their return to work in the UK, these health care workers may be subject to additional health checks (as defined in reference 33) if they may have been exposed to serious communicable diseases while away.
83. In the UK, as well as elsewhere, it is important that all who may perform procedures which involve a risk of significant occupational exposure are well versed in the principles of blood-borne virus infection control precautions (21; 34). These principles should be introduced in medical, dental school and nursing training curricula prior to the start of clinical attachments (34) and, as a minimum, prior to the performance of any invasive procedures such as venepuncture. At the same time, all students should be made aware of the importance of reporting any occupational exposure, so that consideration can be given to the need for PEP. These messages should be reinforced at regular intervals.

84. The risk of nosocomial HIV transmission for health care workers working overseas in low-income countries may be increased by a combination of factors (34–37). Firstly, the relatively much higher prevalence of HIV infection in the patients being cared for than in the UK. Secondly, lack of resources to implement standard infection control measures adequately and poor or inadequate equipment and facilities leading to increased risk of exposure. Thirdly, in the case of students seeking work experience, their relative inexperience/lack of technical skills may increase their likelihood of exposure to blood and other body fluids.
85. Health care workers (including students) intending to work in health care settings overseas should be advised about health and safety issues when working outside the UK, including the risk of occupational and other exposure to HIV.
86. Medical, dental and nursing schools should consider developing accessible, regularly updated advice for students considering electives overseas about measures to keep the risk to their health to a minimum, including information about PEP (36–38). Specific consideration should be given to the risk of occupational exposure to HIV and how to minimise this.
87. Advice should include up-to-date information about the prevalence of HIV infection in the country that a student is considering for an elective. Students considering electives in high HIV prevalence situations should be made aware of the occupational consequences in terms of ability to pursue a career involving exposure-prone procedures (31; 33). Some medical schools may advise students against involvement in clinical procedures that carry the highest risk of occupational exposure – for instance in surgery or obstetrics – in areas of high HIV prevalence.
88. Pre-travel briefing might include reinforcement of advice on immediate post-exposure first aid measures (see paragraph

23), and training on self-assessment of occupational exposure (i.e. whether an exposure is or is not significant with the potential to transmit HIV) as considered earlier in this document (paragraph 26). Advice should also be given about how to make some assessment of the likelihood of HIV infection in the source, as many people who are infected with HIV in less developed countries will not have had their infection diagnosed.

89. Procedures should be clarified for access to urgent advice in the event of any significant occupational exposure to a source considered likely to have HIV infection. Even if not working in a major centre, it may be possible for arrangements to be in place for advice to be obtained as soon as practicable at the nearest major centre, or alternatively by telephone from the UK source of expert advice to their own employer/medical school.
90. Employers and medical, dental and nursing schools should consider making 7-day starter packs of PEP drugs available to workers/students travelling to countries where antiretroviral therapy is not commonly available. These packs should include the same triple PEP regimen as recommended for use in the UK. The more widespread use of antiretrovirals in resource-poor settings has increased the likelihood of occupational exposure to resistant virus, making a triple PEP regimen necessary. Any student/other worker issued with a starter pack including a protease inhibitor should be warned about increased toxicity in the event of dehydration.
91. The principles about starting PEP as soon as possible after a significant occupational exposure, and the known short-term and unknown long-term adverse effects, should be made clear to those issued with PEP drugs.
92. In circumstances where it has been considered necessary to start PEP, expert advice by phone will also be needed to help the student/other worker decide whether the regimen needs

to be continued for four weeks and, if so, about the need for urgent repatriation. This may be appropriate if further treatment and follow-up cannot reasonably be accessed in the foreign country. The possibility of insuring against the need for repatriation in the event of a medical emergency requiring treatment should be explored with the travel insurance provider, prior to leaving the UK.

93. It is important that the possibility of occupationally acquired HIV infection is specifically considered after occupational exposure in countries of high HIV prevalence, and excluded before performing exposure-prone procedures in the UK (33). On return from working abroad in countries where they may have been exposed to serious communicable diseases, all health care workers, including students, should undergo an occupational health risk assessment, as recommended in reference 33. After discussion of the risk(s) to which they may have been exposed, HIV testing may be considered appropriate (in reference 31 – paragraphs 4.8–4.9). Of the 14 'possible' occupationally acquired HIV infections reported in the UK, 13 health care workers had worked in areas of high HIV prevalence (specifically, Africa and the Indian Sub-continent) and were probably infected abroad (29).
94. The outcomes of such risk assessments will help medical, dental and nursing schools steer future students away from placements for electives where the risks to which they may be exposed – e.g. by poor facilities for protecting themselves against blood-borne viruses – outweigh the possible benefits otherwise perceived.

## Chapter 5: Exposure outside the hospital setting

95. For the purposes of this document, 'outside the hospital setting' refers to exposures in the wider community, such as might occur through sharing of drug injecting equipment with someone with HIV or injury resulting from contact with a discarded needle. Sexual exposure to HIV is specifically excluded from this document because separate detailed guidance is available from the British Association for Sexual Health and HIV (BASHH) (3). (See: <http://www.bashh.org/documents/58/58.pdf>) EAGA endorses the BASHH guidance as an authoritative interpretation of the available evidence.

### 5.1 Equity of access and management

96. Primary care trusts (PCTs) are responsible for commissioning occupational health services for their own staff and for GPs and dentists and their staff in the PCT area. This is usually achieved by means of a contract with a local NHS occupational health service. Services for the general public are typically provided by A&E departments or GUM clinics. These are the arrangements for England. Similar ones, reflecting local health service structures, are in place in the other countries of the UK. Provision of monitoring and follow-up for health care workers taking PEP will therefore vary according to local arrangements.
97. All inoculation injuries with the potential to transmit HIV, whether they occur in the community, in a health care environment, to a health care worker or another individual, should be managed in the same way. An individual risk assessment of the circumstances of the exposure should be conducted and this, along with the other considerations detailed in this guidance, must form the basis for deciding whether PEP is started.

98. Owing to the complexity of the risk assessment process and the desirability of having PEP prescribed by a physician experienced in the use and monitoring of antiretroviral medications (for side effects, drug interactions etc), occupational health services (backed up by other services as required) have been identified as the main providers of occupational PEP.
99. However, where a GP is responsible for providing occupational health cover for a practice or group of practices he/she may prescribe at least a starter pack of PEP, before referring the exposed person to an HIV physician for monitoring and follow-up.
100. Inoculation injuries with the potential to transmit HIV may also place the individual at risk of other blood-borne virus infections (e.g. hepatitis B and C). Testing and follow-up for other infections as appropriate should be undertaken, and the need for post-exposure prophylaxis for hepatitis B should be considered.

## 5.2 Other occupational groups

101. Those responsible for occupational health provision to other professional groups who may be at some risk of exposure to HIV-infected material outside health care settings (e.g. police, fire service, prison service, voluntary aid agencies and the armed forces) may wish to use these guidelines as a basis for developing guidance appropriate to the particular occupational setting.
102. A working group has issued advice to the Scottish Executive on protecting front-line workers (police, prison and fire and rescue service staff) and victims of crime from blood-borne viral infections and from anxiety about them (5).

## 5.3 Children

103. If a child has been exposed, specialist advice from a paediatrician experienced in the field of HIV should be



sought. PEP guidelines for children exposed to blood-borne viruses can be found on the website of the Children's HIV Association of UK and Ireland (<http://www.chiva.org.uk/protocols/pep.html>).

#### 5.4 Factors affecting use and efficacy of non-occupational PEP

104. Factors affecting the use of non-occupational PEP include the probability of HIV infection in the source (e.g. the injecting equipment sharer or discarded needle), the likelihood of transmission by the particular exposure and the interval between the exposure and presentation for PEP. The efficacy of non-occupational PEP depends on the drugs used (especially if exposure was to resistant virus), the exposed person's adherence to the PEP regimen and whether the incident was isolated or recurrent (3).
105. From the point of a decision being reached that it is appropriate to prescribe PEP after non-occupational exposure, all the same considerations apply as for occupational exposure. In addition, there may be a need for counselling to prevent recurrence (e.g. where exposure occurred through sharing of drug injecting equipment).

## **Annex A: Body fluids and materials which may pose a risk of HIV transmission if significant occupational exposure occurs**

Amniotic fluid

Blood

Cerebrospinal fluid

Exudative or other tissue fluid from burns or skin lesions

Human breast milk

Pericardial fluid

Peritoneal fluid

Pleural fluid

Saliva in association with dentistry (likely to be contaminated with blood, even when not obviously so)

Semen

Synovial fluid

Unfixed human tissues and organs

Vaginal secretions

Any other body fluid if visibly bloodstained

## Annex B: General Medical Council (GMC) guidance

The guidance in this annex is provided by the GMC.

### **Good Medical Practice (2006) (39)**

79. *If you know that you have, or think that you might have, a serious condition that you could pass on to patients, or if your judgement or performance could be affected by a condition or its treatment, you must consult a suitably qualified colleague. You must ask for and follow their advice about investigations, treatment and changes to your practice that they consider necessary. You must not rely on your own assessment of the risk you pose to patients.*

### **Serious Communicable Diseases (1997) – extract from GMC website<sup>3</sup>**

The GMC guidance on *Serious Communicable Diseases* (1997) was withdrawn on 13 November 2006. In response to a number of recent inquiries, this is a reminder that the issues covered in the 1997 guidance are dealt with in other GMC guidance or are now governed by legislation.

Current GMC advice on consent to testing can be found in *Seeking Patients' Consent: the ethical considerations* (recently replaced by *Consent: patients and doctors making decisions together*). Our advice on disclosure of confidential patient information to third parties (such as a person's infection status) can be found in *Confidentiality: protecting and providing information*.

Decisions about testing the infection status of incapacitated patients, after a needle-stick or other injury to a healthcare worker, must take account of the current legal framework governing capacity issues and the use of human tissue. In

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3 See: [http://www.gmc-uk.org/guidance/serious\\_communicable\\_diseases/index.asp](http://www.gmc-uk.org/guidance/serious_communicable_diseases/index.asp)

England, Wales and Northern Ireland this area is covered by the Human Tissue Act 2004 and the Mental Capacity Act 2005 (E&W only). In Scotland this area is covered by the Adults with Incapacity (Scotland) Act 2000 and the Human Tissue (Scotland) Act 2006. As we understand it, current law does not permit testing the infection status of an incapacitated patient solely for the benefit of a healthcare worker involved in the patient's care. Concerns about how best to care for healthcare workers who may have had high risk exposure to a serious communicable disease, where the patient's infection status is not known, should be raised with local occupational health advisers, and legal advice should be sought where necessary.

### **Further information**

Legislation: Office of Public Sector Information

Human Tissue Regulations: Department of Health

Human Tissue Codes of Practice: Human Tissue Authority

Mental Capacity Codes of Practice: Ministry of Justice

Adults with Incapacity (Scotland) Act 2000 – Legislation and Codes of Practice: Scottish Executive

## Annex C: What to prescribe for PEP

1. Antiretroviral agents from three classes of drug are currently licensed for first-line treatment of HIV infection, namely:
  - nucleoside/nucleotide analogue reverse transcriptase inhibitors (NRTIs);
  - non-nucleoside reverse transcriptase inhibitors (NNRTIs); and
  - protease inhibitors (PIs).
2. Zidovudine (an NRTI) is the only drug to date which has been studied and for which there is evidence of a reduction in risk of HIV transmission following occupational exposure (9).<sup>4</sup> However, as no antiretroviral drug has been licensed for PEP, they can only be prescribed for PEP on an 'off-label' basis.
3. In HIV-infected patients, triple therapy has proved more effective than mono- or dual-therapy in suppressing HIV replication and avoiding the emergence of viral resistance. The US guidelines recommend two-drug PEP regimens following lower-risk incidents and three-drug regimens only for higher risks (14). This two-tier approach adds to the complexity of the risk assessment process, at the expense of greater potency and protection for the exposed worker, and is not recommended by EAGA. The main arguments in favour of two-drug PEP (fewer side effects, better adherence and course completion rates) (40) are being addressed through switching to better-tolerated agents with lower pill burdens. At the same time, a potent three-drug PEP regimen is preferred because resistance to antiretroviral drugs is found at significant levels in both treated and untreated infected individuals in the UK (10; 11).

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4 Zidovudine is no longer recommended for PEP starter packs, preference being given to newer drugs with better tolerability.

- Information about the virus present in the source patient and, if known, any sexual partner of the source patient will be relevant when choosing appropriate PEP drugs. Similarly, information about the source patient's (and his or her sexual partner's) previous and current antiretroviral therapy may also be important. Any information available in the source patient's medical record about antiretroviral drug resistance should be used to inform the choice of PEP drugs (see Annex E).

### Starter regimen

- After due consideration of storage/stability issues, side-effect profiles (41–43), drug interactions, drug resistance and regimen simplicity (i.e. reduced pill burden and food restrictions), the following regimen is now recommended for PEP starter packs:<sup>5</sup>

One Truvada tablet (300mg tenofovir and 200mg emtricitabine (FTC)) once a day

*plus*

Two Kaletra film-coated tablets (200mg lopinavir and 50mg ritonavir) twice a day

- There are no food restrictions associated with this regimen and the PEP pack can be stored at room temperature.
- This new regimen is also consistent with the generic regimen of two NRTIs plus boosted PI recommended for PEP following non-occupational exposure (3). All primary care trusts in England have been directed to make PEP available for their local populations as part of sexual health services (4). Harmonisation of the regimens for occupational and non-occupational PEP has the potential to simplify access arrangements.

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<sup>5</sup> Truvada plus Kaletra is the preferred regimen, but Combivir plus Kaletra may be considered as an option if there are difficulties sourcing starter packs containing Truvada. Due to concerns about long-term stability outside the original container, some Prepacking Units may be unable to supply starter packs containing Truvada.

8. While the above regimen is recommended for emergency starter packs, other NRTI and PI combinations could be used where the physician considers them more appropriate for individual patients. Other new classes of drugs, such as entry inhibitors and integrase inhibitors, may have a role in cases of resistant source virus, but there is currently no evidence for their use in this situation.

## Side effects

9. All of the antiretroviral agents have been associated with side effects. Many of these can be managed symptomatically. Side effects of the NRTIs (e.g. tenofovir and emtricitabine) include gastrointestinal (e.g. nausea, diarrhoea) as well as dizziness and headache. In clinical trials of Kaletra, the most commonly reported side effect was diarrhoea, followed by other gastrointestinal disturbances, asthenia, headache and skin rash (44).
10. Those providing advice on and protocols for prescribing PEP should maintain awareness of advances in HIV therapeutics, potential side effects, adverse drug reactions and drug interactions, and seek further expert advice where necessary. Prescribers need to be aware of the greater potential for drug interactions between Kaletra (due to the ritonavir component of the formulation) and other prescription and non-prescription medicines (relative to the PIs previously recommended for PEP) and counsel patients accordingly. For sources of further advice about drug interactions, see Annex F.
11. Inclusion of an NNRTI in PEP regimens (occupational or non-occupational) is not recommended. Both of the NNRTIs licensed for treatment of HIV infection in the UK (nevirapine and efavirenz) are associated with short-term toxicity: nevirapine has the potential to cause severe rashes (which may be confused with rash associated with HIV seroconversion) and sometimes Stevens–Johnson syndrome;

efavirenz is associated with neurological side effects and is also contraindicated in pregnancy, but it has a lower incidence and severity of rash than nevirapine. Serious adverse events (including life-threatening hepatotoxicity) have been reported in health care workers taking nevirapine as part of PEP (45; 46). There is evidence of incremental improvement in tolerability of PEP regimens as the protease inhibitor component has evolved (i.e. Kaletra replacing nelfinavir which replaced indinavir) with a stable zidovudine/lamivudine backbone (47).

12. If symptoms believed to arise from PEP are distressing and cannot be managed symptomatically and the health care worker feels unable to continue to adhere to the regimen, expert advice should be sought about suitable substitutions. This process should be informed, as before, by considerations of the source patient's antiretroviral history if known.
13. Adverse reactions associated with antiretroviral drugs should be reported using Yellow Cards (available in the back of the British National Formulary) to:

Medicines and Healthcare products Regulatory Agency  
CHM Freepost  
London  
SW8 5BR

Telephone: 0800 731 6789 or 020 7084 2000

Alternatively, Yellow Cards can be completed via the website: <http://www.yellowcard.gov.uk>

14. Any drug regimen should take into account the following factors:
  - whether the health care worker is or may be pregnant (see Annex E);
  - whether the health care worker has an existing medical condition;



- the potential for interaction with other medications (see Annex F); and
- the possibility that the virus may be resistant to one or more of the drugs, or where the exposed health care worker has been handling resistant virus in a laboratory (see Annex E).

**In all these circumstances expert advice should be sought.**

15. There may be local variations in the choice of regimen used. As newer antiretroviral drugs are developed, it is likely that other drugs will become the preferred regimen for PEP. Managers should ensure that PEP policies and protocols reflect current best practice.

# Annex D: Reporting of occupational exposures to HIV

## Reporting to HPA Centre for Infections (Cfi) or, in Scotland, to Health Protection Scotland (HPS)

1. Occupational health physicians and clinicians involved in the care of health care workers are encouraged to report occupational exposure to HIV (in complete confidence) to Cfi or HPS. By doing this, central data can be analysed so that:
  - the size of the problem and the degree of risk can be quantified;
  - working practices and procedures which are particularly risky may be identified; and
  - the side effects and benefits of prophylaxis may be assessed.
2. To report an occupational exposure in England, Wales or Northern Ireland to the surveillance scheme, please contact the Occupational Exposure Surveillance Team, HIV/STI Department, HPA Centre for Infections, 61 Colindale Avenue, London NW9 5EQ (Tel. 020 8327 7095). It is anticipated that a reporting system in Scotland will be implemented in 2008. Health care professionals should contact the HIV/STI Team, HPS, Clifton House, Clifton Place, Glasgow G3 7LN (Tel. 0141 300 1100) for further details.
3. Background to the surveillance scheme and summaries of the data collected can be found at: [http://www.hpa.org.uk/infections/topics\\_az/bbv/occ\\_exp.htm](http://www.hpa.org.uk/infections/topics_az/bbv/occ_exp.htm)

## Reporting of occupational exposure to HIV to the Health and Safety Executive (HSE)

4. In the event of exposure to HIV, employers may be required to report the event to HSE under the Reporting of Injuries, Diseases and Dangerous Occurrences (RIDDOR) Regulations 1995. The most likely requirement, if any, may be the need to report a **dangerous occurrence**; namely *"Any accident or incident which resulted or could have resulted in the release or escape of a biological agent likely to cause severe human infection or illness."*
5. Cases of HIV infection resulting from exposure in the health care setting will also normally be reportable as **diseases** within the meaning of RIDDOR, i.e. resulting from *"work with micro-organisms; work with live or dead human beings in the course of providing any treatment or service in conducting any investigation involving exposure to blood or body fluids; work with animals or any potentially infected material derived from any of the above."*
6. HSE have an InfoLine (0845 345 0055) for general queries relating to RIDDOR or COSHH. Reports under RIDDOR can be made by contacting the Incident Contact Centre on 0845 300 9923 (Monday to Friday 8.30am to 5.00pm) or electronically via the HSE website <http://www.hse.gov.uk/riddor/index.htm>

## Serious Untoward Incident reporting system

7. In England, reporting of Serious Untoward Incidents associated with infection should be via the normal reporting system for all Serious Untoward Incidents, from the trust to the strategic health authority for onward reporting as appropriate. Further details can be found in Department of Health guidance (48). Similar arrangements, reflecting local health service structures, are in place in the other countries of the UK.

# Annex E: PEP: special circumstances

## Viral drug resistance

### Source patient

1. For known positive sources, information about drug resistance should be used to guide decisions about PEP. Resistance should be suspected if there has been prolonged treatment with any antiretroviral, where there is clinical progression of disease or a persistently increasing viral load and/or a decline in CD4 lymphocyte count despite therapy, or a lack of virological response to a change in therapy.
2. The HIV-infected source patient will fall into one of these categories:
  - hitherto undiagnosed; in this case, prevalence of resistance to any class of drug can be estimated as 5–10% (11);
  - already diagnosed, and untreated; these patients are increasingly likely to have had a resistance test undertaken, since baseline testing is recommended (49);
  - on treatment with undetectable viral load; they will be of very low infectivity, and will also probably have had a baseline resistance test;
  - on treatment with detectable viral load; they are likely to have resistant virus and also a recent resistance test.
3. Resistance is not all or none, and the drugs recommended for the PEP starter pack – tenofovir/emtricitabine and lopinavir/ritonavir – will retain useful activity against the most common resistant viruses in the UK. Therefore, concerns over resistance should not delay standard PEP, which should be initiated as soon as possible after the incident.

4. In US and Brazilian studies, a high prevalence of drug-resistant HIV has been found among source patients for occupational HIV exposures (50; 51). It is therefore important to take account of the results of a previous resistance test. If this suggests the standard PEP regimen would be poorly effective, treatment should be altered, taking account of the views of an expert in antiretroviral therapy/drug resistance.

### **Laboratory staff**

5. In the case of exposure of laboratory-based staff who work with drug-resistant virus, either because of routine resistance testing or research work on live viruses, there must be provision within local PEP protocols to obtain an immediate expert opinion on appropriate treatment.

### **Pregnancy**

6. Pregnancy does not preclude the use of HIV PEP. Expert advice should always be sought if PEP is considered indicated for a female health care worker who is pregnant, after assessment of the circumstances of the exposure and of the source patient. Urgent pregnancy testing should be arranged for any female worker who cannot rule out the possibility of pregnancy, as part of the evaluation prior to the exposed worker reaching a personal, informed decision about starting PEP.
7. The British HIV Association has published guidelines for prescribing antiretroviral therapy in pregnancy (52). There has been no indication of particular problems for the babies of HIV-infected women who have become pregnant while already on antiretroviral medication. It should be noted that there is limited experience of the use in pregnancy of some of the newer drugs.

8. A pregnant health care worker who has experienced an occupational HIV exposure should be counselled about the risks of HIV infection, about the risks for transmission to her baby, and about what is known and not known about the potential benefits and risks of antiretroviral therapy for her and her baby, to help her reach an informed personal decision about the use of PEP.
9. Decisions on the use of specific drugs in pregnancy may be influenced by their individual adverse effects. For example, drugs that may cause nausea may exacerbate pregnancy-associated nausea. Efavirenz is contraindicated in pregnancy and not recommended for inclusion in PEP regimens (see Annex C).

## Annex F: Interactions of antiretroviral medications with commonly used medicinal products

1. Antiretroviral medications may have potentially serious interactions with other prescription or non-prescription drugs. These can affect patient safety and the effectiveness of prophylaxis. Information on interactions changes rapidly with advances in therapeutics, so it is important to use up-to-date sources. **It is always advisable to check with a pharmacist.**

### Sources of information

- Summary of product characteristics for the specified medicinal products
- British National Formulary
- Interaction charts produced by the Liverpool HIV Pharmacology Group (<http://www.hiv-druginteractions.org/>)

# Annex G: PEP for patients after possible exposure to an infected health care worker

## Blood exposure incidents

1. Implementation of the recommendations in *HIV infected health care workers: Guidance on management and patient notification* (31) and in *Health clearance for tuberculosis, hepatitis B, hepatitis C and HIV: new healthcare workers* (33) will serve to minimise the risks that a patient may be exposed to the blood of an infected health care worker. Firstly, the restriction of HIV-infected health care workers from performing exposure-prone procedures minimises the likelihood of the health care worker sustaining an injury with the potential for transmission. Secondly, any health care worker who believes they may have been exposed to infection with HIV, in whatever circumstances, must promptly seek and follow confidential advice on whether they should be tested for HIV. Failure to do so may breach the duty of care to patients. Therefore health care workers are under a continual obligation to assess their own risk. New health care workers who will perform exposure-prone procedures are tested for HIV.
2. Four distinct scenarios can be envisaged that may result in a patient being exposed to HIV-infected blood from a health care worker or other patient:
  - during an exposure-prone procedure performed by a health care worker who does not know his/her HIV status;
  - during a non-exposure-prone procedure performed by an HIV-infected health care worker (e.g. physical assault on the health care worker, spontaneous nosebleed);



- where a health care worker accidentally sticks themselves with a needle and then puts the needle in the patient without realising what has happened; and
- in the unlikely event that an invasive device or product contaminated by use on one patient is accidentally re-used on another patient.<sup>6</sup>

Appropriate management of such potential exposure incidents will further reduce the risk of infection for patients.

3. The General Medical Council's guidance *Good Medical Practice* (39) (see Annex B) states that doctors infected with blood-borne viruses should not rely upon their own assessment of the risks they pose to patients. Any doctor is bound to take all proper steps to safeguard the interests of his/her patients and this would include ensuring that, following an exposure incident, he/she co-operates fully with those conducting the risk assessment, providing all necessary information about their own infection status or risk behaviour.
4. Every employer should draw up a policy on the management of blood exposure incidents. In accordance with guidance on the management of HIV-infected health care workers (31), each NHS body should designate one or more doctors<sup>7</sup> to whom health care staff or any other person present in the health care setting may be referred immediately for advice if they have been exposed, or have exposed others, to potentially infected blood. The designated doctor(s) needs to be of sufficient seniority (consultant level) and arrangements for adequate out-of-hours cover also need to be in place. Local policies should specify who will be responsible for provision of PEP

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6 Potential patient-to-patient transmissions should be assessed following usual guidance on source patient testing (see Section 2.3).

7 Examples include clinical specialists in Occupational Health, Public Health, Infectious Diseases and Microbiology. All need to be trained in conducting risk assessments and appropriate use of PEP.

and for the follow-up of staff or patients who have been exposed.

### Assessment of incidents

5. Circumstances that could allow the transmission of blood-borne viruses from health care worker to patient include:
  - visible laceration<sup>8</sup> occurring to a health care worker's hand in circumstances where the patient's open tissues or mucous membranes could be contaminated with the health care worker's blood;
  - visible bleeding of a health care worker from any other site (e.g. nosebleed) leading to significant bleed-back into a patient's open tissues or mucous membranes; and
  - an instrument or needle contaminated with the blood of the health care worker being inadvertently introduced into the patient's tissues.
6. Where any health care worker is involved in, or observes, any of the above incidents, that health care worker should take the following actions:
  - The injured person should stop the procedure as soon as reasonably practicable, wash and dress the wound and stem the bleeding.
  - Report the incident to the clinical supervisor or line manager or other person responsible according to local policies.
  - Ensure that, in accordance with local policy, the Occupational Health department, infection control officer or other nominated individuals are informed without delay.
  - Complete an accident/incident form.

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8 Most needlestick/puncture wounds would be excluded from consideration unless they resulted in significant bleed-back into the patient.

7. Local policies on recording critical incidents should be followed. In the surgical setting, it is good practice to record injuries to health care workers in operating theatre records and standard procedure for a preliminary risk assessment on the injured health care worker to be conducted by another member of the clinical team. This should include ascertaining whether visible blood is present that is likely or believed to be the health care worker's. Where the incident is not considered to be a significant blood exposure, this assessment must be recorded in the theatre record.
8. If, following a preliminary assessment, further risk assessment is warranted, this should be undertaken by the designated doctor (see paragraph 4 above) without delay to decide whether a significant exposure of the patient to the health care worker's blood has occurred. Where the incident is not considered by the designated doctor to be a significant blood exposure, no further action is required. The designated doctor's assessment should be entered in the health care worker's occupational health record and critical incident report if appropriate.
9. If the incident is considered to be a significant blood exposure, involving bleed-back into the patient, the injured health care worker should routinely be asked to consent to testing for HIV, hepatitis C and hepatitis B (where status not already known). Injuries resulting in overt bleeding will occur rarely. HIV testing of the health care worker should be conducted urgently, with the results available ideally within 8 hours of the exposure incident to maximise the benefit of PEP if indicated.<sup>9</sup>

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9 No PEP is currently available for hepatitis C. However, early treatment of acute hepatitis C infection may prevent chronic hepatitis C infection (53). Follow-up of exposed patients should follow that described in management for occupational exposure to hepatitis C (54). A course of hepatitis B vaccination with or without immunoglobulin may be recommended as PEP following exposure to hepatitis B (21).

10. Normalising the request to test for HIV (and hepatitis C) overcomes difficulties of making judgements about personal behaviour and risks and avoids stigmatising health care workers. The normal principles of confidentiality and informed consent apply. Pre-test discussion should cover both occupational and personal implications of a positive test result.
11. To encourage health care worker compliance with testing and reporting incidents, reporting policies should safeguard the health care worker's confidentiality (e.g. anonymised reports are adequate; the health care worker's identity should only be disclosed to those who need to manage the incident and the incident should be noted in their personal occupational health record).
12. If the health care worker tests positive for any blood-borne virus, the patient should be notified of an intra-operative exposure without revealing which member of the clinical team is infected. Incidents that entail informing patients should be reported to the National Patient Safety Agency. PEP for HIV (see 'Use of PEP' below) should usually only be offered and recommended following a positive test in the health care worker. Health care workers are presumed to be at low risk for HIV infection (55). There are also considerable practical difficulties in administering PEP in the immediate post-operative period (e.g. obtaining valid consent, possible need for parenteral administration and toxicity of PEP for sick patients). Only in exceptional circumstances (e.g. the health care worker is considered to be at high risk of HIV infection and/or refusal of the health care worker to be tested) would it be warranted to initiate PEP in the absence of a positive HIV test result.
13. If the health care worker tests negative for blood-borne viruses, there is no need to inform the patient about the incident and this would also avoid causing the patient unnecessary anxiety. A written record of the incident and

test results should, however, be entered in the health care worker's occupational health notes.

14. Where an incident occurs outside an exposure-prone setting involving a health care worker who is known to be HIV positive, the incident should be discussed in confidence by the designated doctor and the clinician responsible for the care of the patient. Where the clinician responsible for the care of the patient is also the injured health care worker, then another senior clinician should be consulted. These parties will make a decision about the management of the exposed patient. Where active management is indicated, the patient should be informed that an exposure may have occurred. The patient should then be managed in accordance with current guidelines for the management of exposure incidents to HIV-infected blood, including obtaining a baseline serum specimen from the patient for storage. This information should be recorded in the patient's notes.
15. Members of the infection control team should have access to confidential or anonymised copies of risk assessments performed following significant exposures for regular audit.

### Use of PEP

16. Where a patient has been accidentally exposed to the blood of a health care worker who is known or found to be HIV infected, then PEP is **recommended**. A 28-day course of treatment with a triple combination of antiretroviral drugs is normally used and needs to be commenced rapidly for maximum efficacy (see Section 3.3).
17. Particular consideration will need to be paid to the risk/benefit ratio of PEP for sick patients whose ability to tolerate antiretroviral therapy may be compromised. A higher threshold for commencing PEP may be appropriate because of the high incidence of side effects. Advice from an HIV specialist on the best combination to use may be necessary

for patients with systemic organ failure/organ insufficiencies. Advice on dose modification and formulations should be sought from an HIV specialist pharmacist.

### Follow-up of patients exposed to HIV-infected blood

18. The guidance on follow-up for health care workers occupationally exposed to HIV should be applied to all patients who suffer a significant exposure to known HIV-infected blood, regardless of whether they have received PEP (see Section 3.3).

### Special considerations

#### The health care worker who refuses a blood test

19. It would be unlawful to compel a health care worker to take a blood test. However, an employer may take appropriate steps to protect patients from a worker who refuses to undergo a test following an incident, such as thereafter restricting him/her from performing exposure-prone procedures.

#### The unconscious patient

20. PEP should not be withheld from an unconscious patient on the grounds that they are unable to consent, if clinical judgement deems it to be in their best clinical interests.

#### The nil-by-mouth patient

21. Antiretroviral drugs are available in a number of formulations suitable for naso-gastric or intravenous administration (see Table 1). Combinations of antiretrovirals for use as PEP in nil-by-mouth patients are therefore unlikely to differ significantly from standard currently recommended regimens (see Annex C).

**Table 1: Antiretroviral formulations suitable for naso-gastric or intravenous administration**

Drug	Strength	Route of administration <sup>1</sup>	Special requirements
<b>Nucleoside reverse transcriptase inhibitors</b>			
Abacavir oral solution	20mg/ml	Naso-gastric	HLA B*570 testing required beforehand and therefore not suitable
Didanosine tablets	200mg	Naso-gastric	Disperse in water. Adult dose >60kg is 2 tablets (400mg). Seek advice from pharmacist for other dosing
Emtricitabine oral solution	10mg/ml	Naso-gastric	Liquid has lower bioavailability than capsules therefore not equivalent mg for mg
Lamivudine oral solution	10mg/ml	Naso-gastric	
Stavudine powder for oral solution	1mg/ml	Naso-gastric	
Tenofovir tablet	245mg	Naso-gastric	Crush tablet and dissolve in 100ml water (may take up to 20 minutes to dissolve). Administer immediately
Truvada tablet	245mg tenofovir and 200mg emtricitabine	Naso-gastric	Crush tablet and dissolve in 100ml water (may take up to 20 minutes to dissolve). Administer immediately
Zidovudine oral syrup	50mg/5ml	Naso-gastric	
Zidovudine injection	10mg/ml	Intravenous	

Drug	Strength	Route of administration <sup>1</sup>	Special requirements
<b>Protease inhibitors<sup>2</sup></b>			
Fosamprenavir oral solution	50mg/ml	Naso-gastric	
Lopinavir with ritonavir oral solution	Lopinavir 400mg and ritonavir 100mg in 5ml	Naso-gastric	
Ritonavir oral solution	400mg/5ml	Naso-gastric	
<b>Non-nucleoside reverse transcriptase inhibitors<sup>3</sup></b>			
Nevirapine oral suspension	10mg/ml	Naso-gastric	
Efavirenz oral liquid	30mg/ml	Naso-gastric	Liquid has lower bioavailability than capsules therefore not equivalent mg for mg

Notes: 1. Data are limited on adsorption via naso-gastric route for all drugs mentioned.

2. No stability data available on administering atazanavir via naso-gastric route.

3. See Annex C paragraph 11 for caveats around the use of non-nucleoside reverse transcriptase inhibitors.



## Annex H: Summary of evidence on maximum interval between exposure and commencing PEP

1. In the absence of randomised studies addressing the interval between a risk incident and initiation of PEP, three lines of evidence provide guidance: (i) animal studies; (ii) human perinatal transmission studies; and (iii) consideration of virological/immunological studies on the natural history of primary infection.
2. Firstly, the ability of PEP to prevent infection has been studied in the macaque animal model. Thus, infection of this species with simian immunodeficiency virus (SIV) through the intravenous route, or HIV-2 through the intravaginal route, was shown to be prevented when tenofovir was administered subcutaneously within 12 hours of infection and continued for 28 days (56–58). When treatment was delayed by 48 or 72 hours in the SIV/macaque experiments, only a proportion of animals were protected from infection. Further, a treatment duration of 3 or 10 days, rather than 28 days, was also associated with reduced levels of protection. By contrast, in one study, PEP with intravenous zidovudine, lamivudine and indinavir as early as 4 hours post-infection in an SIV/HIV chimera (SHIV) infection of macaques did not prevent infection (59).
3. One human perinatal transmission intervention study is also informative. In a subset of participants in the ACTG 076 protocol, where antenatal treatment of the pregnant woman with zidovudine was omitted (through choice or limited clinical care), neonatal zidovudine started within 48 hours of birth was associated with an HIV transmission rate of 9.3%, compared with a rate of 18.4% when zidovudine was started at a later time (60).

4. Recent studies of the SIV-macaque model, as well as natural history studies following HIV-1 transmission in humans, demonstrate extensive infection of gut-associated CD4 lymphocytes, and their preferential depletion is evident at the time of primary infection. This suggests there is only a brief window of opportunity to prevent or abort infection (through administering PEP) before irreversible systemic infection and HIV seroconversion occur (61; 62).
5. Together, these studies provide some evidence that PEP is most likely to be effective when initiated as soon as possible (within hours, and certainly within 48–72 hours of infection), and continued for at least 28 days. It should be noted that the evidence base on which these conclusions are based is limited.

# Annex I: EAGA PEP Working Group membership

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