Introduction

A Joint ILO/WHO Technical Meeting for the Development of Policy and Guidelines on Occupational and Non-occupational Post-exposure Prophylaxis for HIV Infection (HIV-PEP) was held in Geneva from 5 to 7 September 2005. The aim of the meeting was to review existing evidence and experience on occupational and non-occupational HIV-PEP and to formulate a consensus to developing HIV-PEP guidelines and policies.

For feasibility and affordability, the primary focus of the guidelines will be on occupational and sexual assault exposures. The needs of target populations will be addressed whenever possible.

Review of current practice: key points from the background presentations

HIV-PEP efficacy and cost-effectiveness

- Since HIV-PEP is not 100% effective, the importance of primary prevention must be reinforced.

- The efficacy of HIV-PEP has been shown in occupational settings, but remains unproven in the non-occupational setting. For ethical reasons there will probably never be a randomized controlled study to evaluate the efficacy of non occupational HIV-PEP; in particular, it is often not possible to identify and test the source of seroconversion, and thus to document HIV-PEP success or failure. The evidence for HIV-PEP efficacy is indirect and based on the findings of studies on primates, post-natal infant studies and a single health-care worker (HCW) case-control study.

- Animal studies suggest that initiating HIV-PEP within 12, 24 or 36 hours of exposure is more effective than initiation within 48 or 72 hours, and that HIV-PEP is not effective when given more than 72 hours following exposure. Furthermore, 28-day course of drug therapy appears to be more effective than courses lasting only 3 or 10 days.

- There are few data to compare the relative efficacies of two and three-drug HIV-PEP. In terms of its cost-effectiveness, however, studies indicate that the superiority of two- versus three-drug regimens relates to rates of completion, side-effects and community levels of resistance.

Occupational HIV-PEP

General findings

- An occupational exposure is defined as a percutaneous, mucous membrane, or non-intact skin exposure to blood or body fluids that occurs during the course of an individual’s employment. This applies to health care workers (HCW) and to non-health workers.

- Over 300 definite cases or possible HCW HIV transmissions have been documented. 90% have occurred in either Europe or North America, regions that collectively account for just 4% of the global burden of HIV infection. It is likely therefore that the figure is an underestimate of the true number of HCW infections worldwide.

- Unless working environments are safe and appropriate prevention measures on HIV-PEP are in place, it will be increasingly difficult to recruit both local and foreign HCWs to serve high prevalence settings.

- While existing guidelines often prescribe the circumstances whereby HIV-PEP should be offered, recommended or not recommended, multiple recommendation levels with respect to indica-
tions and to the number of drugs may be confusing.

- In the occupational setting, HIV-PEP may well be overused. Moreover, three-drug HIV-PEP is often used when two drugs are recommended.

**Legal principles that apply to all workers**

- HIV-PEP policies should apply to all workers exposed to HIV without distinction, irrespective of the sector in which they work (e.g. public or private, in or out the health sector).

- Confidentiality must be maintained with respect to both the exposed worker and the source person.

- Neither HIV testing nor HIV-PEP should ever be mandatory. Informed consent is critical. Workers must consent prior to HIV testing and prior to receiving HIV-PEP. Informed consent to be tested for HIV should also be obtained from the source person.

- It is the employer’s responsibility to provide their workers with information regarding HIV-PEP - how to obtain urgent advice, and how and to whom to report during working hours. Services should be provided at no cost. All workers need access to voluntary counselling and testing (VCT) if there is any risk of occupational HIV exposure.

- The successful implementation of HIV-PEP policy requires social dialogue between employers, workers and their representatives, and government.

- The workplace should be a delivery point for the full range of HIV-PEP services even if the exposure did not result from occupational exposure.

**Policy and operational considerations for implementing occupational HIV-PEP**

- HIV-PEP policies and protocols must define who is responsible for providing HIV-PEP in both public and private health-care settings and what is the best setting to deliver HIV-PEP in and out the working place.

- HIV-PEP procedures need to be clear, well documented and accessible.

- Risk assessment and prevention, within an occupational health and safety behavioural-based strategy, are critical.

- The pre-existence of VCT, wellness and ART programmes helps ensure the correct and timely provision of HIV-PEP.

- The management of HCWs who are potentially exposed to HIV should include immediate first-aid measures, the reporting of the injury to a designated staff member for risk assessment, consideration of other blood-borne infections, risk reduction measures, and arrangements for follow-up. Exposed HCWs should have immediate 24-hour access to advice about HIV-PEP from a designated provider with local expertise.

- HIV-PEP medication starter packs must be readily accessible.

- Needle-stick incident packs are readily accessible, available in casualty, intensive care units and operating theatres. The content includes full instructions for administering HIV-PEP, a 3-day supply of drugs, laboratory specimen tubes and forms, insurance papers, the needle-stick incident register, a HIV-PEP information sheet, a follow-up sheet, procedures for HIV testing, and statutory reporting forms.

- Testing the source patient for blood-borne pathogen infections should only occur if there has been a significant injury. Rapid testing may be useful but in no case should source HIV test results delay risk assessment and the initiation of HIV-PEP if it is otherwise indicated.

- Exposed HCWs should be reassessed within 3-5 days for medication tolerability and toxicity. If further details about the source become available, a risk assessment re-evaluation may also be appropriate.

**Non-occupational HIV-PEP**

**General findings**

- Existing international guidelines differ in their recommendations with regard to the time to HIV-PEP initiation; the implications of unknown source HIV status; which and how many drugs to use; and the intensity of HIV testing and laboratory monitoring. However:

  - The cut-off time for receiving HIV-PEP is most commonly 72 hours; in some guidelines it can be as little as 36 hours.

  - In some guidelines from developed countries, source HIV status is considered differently if it is known (in which case HIV-PEP is recommended) or not known (in which case HIV-
PEP should be considered on a case-by-case basis. In contrast, guidelines addressing sexual assault in high-prevalence settings tend not to distinguish known and unknown source HIV status.

- Many developed countries guidelines recommend 3-drug HIV-PEP while most guidelines from resource-limited settings recommend just two. There is a tendency to recommend 3-drug HIV-PEP when antiretroviral therapy (ART) is in common use in the country or region, or if the source person was previously on ART, since it could increase the risk to exposure to resistant virus.

Across studies of HIV-PEP use in non-occupational settings: the indications for HIV-PEP, the time to HIV-PEP initiation, the number and type of drugs used, adherence, side-effects and seroconversion rates are inconsistent. In most cases, however, follow-up has been poor.

- Risk behaviour has not been shown to increase substantially among HIV-PEP users and in communities where HIV-PEP is available.

- HIV-PEP uptake among sexual assault survivors in most developed countries is low due, in most cases, to low-acceptance rates. Follow-up and completion rates are relatively lower than among men-who-have-sex-with-men (MSM).

- In other settings such as refugee camps, rape survivors report a great value and motivation regarding PEP

Common problems in resource poor settings providing services to sexual assault survivors include insufficiently trained or over-burdened staff, lack of availability of VCT, lack of information about HIV-PEP among police, health-care providers, and other front-line service providers (such as counsellors handling cases of sexual or domestic violence or child abuse and teachers), lack of patient and community information, difficulty with follow-up, and transportation problems. Centralized and decentralized care systems have advantages and disadvantages. Many have recommended that follow-up care be available at, or close to, home.

The introduction of policy and guidelines has had a significant impact on prescribing practices, in that there is a notable increase in prescriptions for very low-risk exposures in response to patient requests.

Experience with sexual assault survivors from Kenya

- In Kenya, post-rape care is coordinated by local nongovernmental organizations (NGOs): Liverpool VCT and Care. Included among the services provided to survivors of sexual assault in health services are emergency contraception (EC), prevention and treatment of sexually transmitted infections (STIs), HIV-PEP, forensic examination and documentation, laboratory testing and counselling.

- Given the breadth of counselling needs (i.e. for trauma and crisis management, HIV prevention, HIV-PEP adherence and legal issues), there is a clear need for more trained counsellors.

- It is important to develop national standards and protocols for official documentation. A national training plan and curricula, as well as quality assurance systems based on the lessons learned with VCT, must also be developed.

- A plan to increase public awareness is necessary.

- The ideal location of service delivery is not clear. Although ideal in some respects, stand-alone centres are not always feasible. It may make more sense to integrate post-rape care with existing services.

- Developing distribution and supply systems within countries for post-rape care kits may be a challenge.

- The human resource and capacity issues associated with developing comprehensive post-rape care systems cannot be underestimated. Financial resources will be required to support training, HIV-PEP provision through ART service systems (or separately), and to create links with other services, including those for maintaining forensic evidence.

Experience with sexual assault survivors from Brazil

- In Sao Paulo, where the overall HIV prevalence is estimated to be 0.65%, a multidisciplinary programme to treat the victims of sexual assault was created in 1997. Although protocols have evolved over the lifetime of the programme, HIV-PEP starter packs are currently provided by the hospital and clients are then referred to the AIDS reference pharmacy, which is part of Brazilian AIDS programme.

- Between May 1997 and April 2004 a total of 55 perpetrators of sexual assault were tested; 16.4% tested positive for
HIV. While this limited set of results is does not necessarily represent HIV prevalence among perpetrators, it is highly likely that HIV infection prevalence in this population is greater than in the general population. In the context of sexual assault, the overall HIV prevalence of 0.65% is very probably an underestimate of the risk.

Trauma physicians report that a lack of training and problems with quality assurance regarding HIV-PEP and sexual assault care have been among the more challenging aspects of programme implementation. The introduction of HIV-PEP kits, which contain both general and specific information about HIV-PEP and HIV ARV drugs, the relevant paperwork, a follow-up appointment date, and a contact number for further advice and guidance, coupled with efforts to forge partnerships between the police, NGOs and health-care units has resulted in improvements in the time to HIV-PEP initiation and in adherence rates.

Legal perspective with sexual assault survivors from South Africa

HIV-PEP should not be provided without informed consent. Informed consent implies that the consenting person must understand the risks and benefits of the proposed intervention. Information provided should thus be appropriate to age, education level and should take into account the context.

Informed consent does not necessarily require written consent. It is the responsibility of the service provider to assess the patient’s state of mind and be comfortable that the patient understands all of the issues.

The issue of consent is especially challenging for children, orphans, adolescents, any person immediately after experiencing trauma, those with mental disabilities, and patients who are unconscious. Nevertheless, it is feasible to develop guidelines that take these situations into account. For example, the South African National Department of Health guidelines specify that in such cases where obtaining informed consent, even from a guardian, may not be feasible within the permitted time window for HIV-PEP, a designated official such as hospital superintendent may provide consent to initiate treatment.

All individuals have the right to confidentiality regarding their medical information, including HIV test results and the use of HIV-PEP.

HIV testing of the source of exposure may result in an unnecessary diversion of resources and could lead to human rights abuses, such as violations of rights to privacy and bodily integrity.

All individuals have the right to enjoy the highest attainable standard of health, a right guaranteed by the several international and regional treaties. This right imposes an obligation on states to take necessary steps for the prevention, treatment and control of epidemic and other diseases, which include “the establishment of prevention and education programmes for behaviour-related health concerns such as sexually transmitted infections (STIs), in particular HIV/AIDS.” In meeting this obligation, states should ensure that appropriate goods, services and information for the prevention and treatment of STIs, including HIV/AIDS, are available and accessible without discrimination.

Policy considerations for non-occupational HIV-PEP

What are the implications of providing HIV-PEP following sexual exposures in high-prevalence countries where exposures are likely to be chronic rather than isolated or episodic?

Should there be risk stratification based upon the likelihood of HIV infection in the source in high HIV prevalence versus low prevalence settings?

Should there be an earlier cut-off time for HIV-PEP initiation, e.g. 24, 36 or 48 hours and should there ever be a later cut-off time, e.g. 7 days?

Decisions about which drugs to use for HIV-PEP must take into account the context of drug availability in prevention of mother-to-child transmission (PMTCT) and ART roll-out programmes. These choices must also take into account implications regarding resistance, supply chains and cost.

Should HIV testing be required in order to access a starter pack or for continuing full course given either lack of availability of VCT and/or a client’s wish to not test?

Are routine baseline and follow-up laboratory tests necessary?

What minimum level of services should be a prerequisite for HIV-PEP programmes?

Specific needs of target populations

South Africa: The Thohoyandou Victim Empowerment
Program (TVEP) an NGO established, in collaboration with the Department of Health, provides 24-hour sexual assault trauma services within two hospitals in a rural region of South Africa, where the prevalence of HIV is around 15%. All rape victims who test negative for HIV and who present within 72 hours of the assault are offered HIV-PEP.

Initially starter HIV-PEP packs were used. As patients frequently failed to return to the centres because of the distances involved, these were discontinued and currently the full 28-day course of HIV-PEP is prescribed. Home visits and monitoring have had a very positive impact on compliance. Limited human and financial resources are the main problems faced by the NGO. Training forensic nurses in sexual assault management is seen as a possible solution to the shortage of expertise. Capacity building among home-based caregivers and ARV service providers is also perceived as being critical.

HIV-PEP in Children

The lack of specialist expertise is of particular concern in the case of children, since medication dosages must be altered according to the weight of the child. Obtaining guardian consent for children at boarding school or for those who are deaf or blind is also very challenging.

In Thailand, the number of child sexual assault victims seen at the Police General Hospital in Bangkok has been steadily increasing over recent years. Over a 4-year period, 2000-2003, 1365 children were counselled and 1205 consented to HIV testing and HIV-PEP. Forty-five per cent met the criteria for HIV-PEP, but only 15% completed the full 28-day course of HIV-PEP. Follow up at six months was also low, just 27%.

HIV-PEP in emergency settings

The need for clinical guidance on sexual assault management and HIV-PEP in the context of emergency situations has become increasingly apparent in recent years. In response to this demand, WHO and the United Nations High Commissioner for Refugees (UNHCR) developed guidelines for clinical management of rape victims in emergencies (updated in 2004) which recommend HIV-PEP. The latter has also been integrated into a reproductive health kit for emergencies.

Programme experience gained in the United Republic of Tanzania indicates that the integration of HIV-PEP services into the medical response for survivors of sexual assault is possible in refugee camps and may even result in an increase in the numbers reporting rape.

In the United Republic of Tanzania, HIV-PEP provision was introduced as part of a package of sexual and gender-based violence (SGBV) services, in a programme jointly coordinated by the United Nations Population Fund (UNFPA), UNCHR and the International Red Cross (IRC). Sexual assault survivors report a great value and motivation regarding HIV-PEP; of the 91 patients who received HIV-PEP during the first six months of the programme, 92% completed the course. Discontinuation resulted from repatriation, the need to travel to the facility (for Tanzanians), and psychosocial problems (e.g. alcoholism). Although 54% reported side-effects, they were not cited as the main reason for HIV-PEP discontinuation.

The main challenges were limited knowledge on ART among providers, incorrect prescribing of paediatric doses, difficulties in providing accurate information on effectiveness, shared confidentiality of HIV test results, shortage of trained-HIV counsellors, and provider perceptions about whether the exposure was consensual or non-consensual and reluctance to prescribe multiple medications (i.e. in addition to emergency contraception and STI prophylaxis). Logistical challenges included unavailability of medications in syrup form (for children) and problems with follow-up.

Building on the achievements of Tanzanian refugee programme, HIV-PEP services were scaled up in eight other countries during the course of 2005. UNHCR plans to incorporate HIV-PEP provision in all their future SGBV programmes.

HIV-PEP for injecting drug users (IDUs)

Globally, up to 10% of all new HIV infections result from injecting drug use (IDU). It is the primary mode of HIV transmission in a number of countries. A variety of factors, including police abuse, interference with needle-exchange services, fear of arrest for possession of syringes, and government opposition to harm reduction services, drive drug users away from HIV prevention and other health services and foster risky practices, such as syringe sharing.

IDU is high among sex workers. Not only do many sex workers inject drugs, but their clients or sex partners may also be IDUs. Many drug users exchange sex for drugs or money to support their habit. The overlap between sex work and injecting drugs heightens the risk of HIV transmission (through needle
sharing as well as sexual transmission) and exposure to police violence and harassment.

IDU is also highly prevalent among prisoners. Needle sharing is common in prisons and further increases the risk of HIV transmission.

Targeted interventions for IDUs, such as the provision of sterile injecting equipment and opiate substitution therapy, have proved effective in preventing HIV transmission. Often referred to as “harm reduction,” these approaches have been endorsed by WHO and UNAIDS as an integral part of HIV prevention and care strategies for IDUs. Countries that have implemented harm reduction measures on a sufficiently large scale have successfully controlled HIV epidemics among IDUs and in the non-injecting populations.

Despite the numerous challenges, there are several potential benefits from developing HIV-PEP programmes that serve IDUs.

IDUs are entitled to the same ame nt and care as other individuals. International law requires states to take affirmative conduct to promote health and to refrain from conduct that limits the ability to safeguard one’s health. Drug users suffer from addiction-related disabilities, restricting harm reduction programmes and access to HIV-PEP (especially where harm reduction services are unavailable) may constitute a form of discrimination in access to health care.

**Considerations in correctional settings**

The prevalence of HIV infection in prisons has been shown to be higher than in surrounding communities. Lack of HIV prevention education, sexual assault and HIV services such as access to sterile syringes or condoms increase the risk of HIV transmission in prisons.

The risk of HIV transmission exists not just for inmates but extends to correctional officers and also to HCW.

**Developing Guidelines for HIV-PEP: Recommendations**

**Policy considerations**

**Points of consensus**

1. Legal and human rights considerations regarding HIV/PEP (including state obligations to ensure the right to the highest attainable standard of health, to protect against violence and its consequences and to protect rights to privacy and bodily integrity) are critical.

2. HIV-PEP policy must be part of comprehensive HIV prevention, occupational health, and post-rape care service policies. Services must be provided as part of a comprehensive prevention package that emphasizes primary prevention.

3. HIV-PEP policies must include clear implementation guidelines.

4. Financing must be available to subsidize the entire HIV-PEP package.

5. HIV-PEP services must be integrated into existing services. They should not be developed in isolation from other prevention or care policies or programmes.

6. A national health department representative must be responsible for developing and implementing the national HIV-PEP plan. Service providers must also be responsible for implementing the plan at each designated institution.

7. Optimal service delivery sites must be identified in each setting.

8. Key service components must be available prior to implementation of HIV-PEP.

9. VCT capacity should be required prior to developing HIV-PEP services in most circumstances.

10. Risk factors for pre-existing HIV infection in the exposed individual need to be addressed as part of VCT. This information needs to be included in the informed consent process when offering HIV-PEP prior to knowing the HIV test result.

11. HIV-PEP is usually not an appropriate prevention intervention in the context of chronic HIV exposure.

12. HIV-PEP should be offered following exposures that are associated with the potential for HIV transmission.

13. The likelihood of HIV infection in a source of unknown HIV status should take into account HIV prevalence in the community and within demographic groups.

14. Information about HIV-PEP and access to services should be available in a non-discriminatory fashion.

**Points to be discussed in context**

1. Should countries’ prioritization of HIV-PEP within their comprehensive prevention package be based on HIV prevalence?

2. Should ART availability for the treatment of HIV-infected individuals be required in order to develop HIV-PEP policy and programmes?

3. Is it ever acceptable to develop occupational HIV-PEP programmes in the absence of programmes to provide HIV-PEP to sexual assault survivors?

4. Should HIV-PEP ever be offered beyond 72 hours of the potential exposure?

5. Should HIV-PEP be offered to sources with unknown HIV status, including alleged perpetrators of sexual assault?
### Operational issues and implementation of HIV-PEP policies

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<th>Points of consensus</th>
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<td>1. The minimum package of services must be adapted to the setting in which HIV-PEP is used, maximizing existing resources and building linkages.</td>
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<td>2. Patients must receive appropriate information about the risks and benefits of HIV-PEP in order to provide informed consent.</td>
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<td>3. Basic HIV-PEP regimens should include two nucleoside/nucleotide analogue reverse transcriptase inhibitors (NRTI). Three-drugs combination should be proposed in cases where drug resistance may be a risk, particularly in occupational settings. Thee regimen will be presented in the guidelines.</td>
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<td>4. A complete course of HIV-PEP includes 28 days of medication.</td>
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<td>5. Medications used for HIV-PEP should be consistent with first-line WHO ART available in the country.</td>
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<td>6. A designated, trained person with the appropriate skills and expertise should dispense HIV-PEP.</td>
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<td>7. Adequate counselling should include:</td>
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<td>- Adherence to treatment and side effects.</td>
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<td>- Behavioral change and risk reduction.</td>
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<td>8. Trauma for sexual assault survivors.</td>
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<tr>
<td>1. Should clients seeking HIV-PEP be able to defer or even decline HIV testing?</td>
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<td>2. How much medication should be dispensed at the initial contact?</td>
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<td>3. Should availability of any other medications be required in order to provide HIV-PEP?</td>
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<td>4. Should any other laboratory testing be required?</td>
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<td>5. Should any follow-up testing be required?</td>
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<td>6. Should the ability to assess for potential HIV seroconversion be required?</td>
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This meeting represented the first step towards the development of global guidelines on occupational and non-occupational post-exposure prophylaxis for HIV infection. WHO is in the process of developing these guidelines which will be fully harmonized with other WHO documents. The guidelines will be available by end 2006.

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