MEETING REPORT

WHO/UNAIDS CONSULTATION FOR LATIN AMERICA AND THE CARIBBEAN | 27-29 APRIL 2011

Ethical engagement of people who inject drugs in HIV prevention trials

JOINT UNITED NATIONS PROGRAMME ON HIV/AIDS

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Note about this report

This report was drafted by Julieta Arosteguy, who elicited and incorporated input from meeting participants on the first and subsequent drafts. Reva Gutnick and Saladin Osmanov edited the draft report. Catherine Hankins revised the final version. This report represents the opinions expressed by the participants of this consultation and does not necessarily reflect the official positions of the World Health Organization or the Joint United Nations Programme on HIV/AIDS.

Acronyms and short forms used in this document

Acronym or short form	Definition
ART	Antiretroviral therapy
CAB	Community advisory board
CDDC	Compulsory drug detention centre
CODAR	Spanish acronym for people who use drugs who are at higher risk of acquiring and transmitting HIV and other sexually transmitted infections (Consumidor de Drogas con Alto Riesgo de adquirir y transmitir VIH y otras infecciones de transmission sanguinea o sexual).
Ethical Considerations	Ethical considerations in biomedical HIV prevention trials guidance document, UNAIDS/WHO (2007)
GPP	Good participatory practice guidelines for biomedical HIV prevention trials, UNAIDS/AVAC (2007)
GP	Guidance point
HVI	HIV Vaccine Initiative
MSM	Men who have sex with men
NGO	Non-governmental organization
NSP	Needle and syringe programme
OST	Opioid substitution therapy
PAHO	Pan-American Health Organization
PWID	People who inject drugs
PrEP	Pre-exposure prophylaxis
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNODC	United Nations Organization for Drugs and Crime
WHO	World Health Organization

Background

On 27-29 April 2011, the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Health Organization (WHO) convened a Latin America and Caribbean region stakeholder consultation to explore regional challenges to meaningfully engaging people who inject drugs in HIV prevention trials and to identify strategies that can be - or have been – successfully employed to creatively and ethically address these challenges. The consultation was held in Buenos Aires, Argentina.

The objective of the consultation was to contribute regional perspectives from Latin American and Caribbean countries towards the development of human rights-based and evidence-informed international ethical guidance for meaningfully engaging people who inject drugs in biomedical HIV prevention trials. The guidance is relevant to socio-behavioural and other HIV prevention research as well.

The Buenos Aires consultation was the third in a series of three meetings convened in different regions that experience a higher risk of HIV transmission originating from and among people who inject drugs. The first consultation was held in Istanbul, Turkey (June 2010) with a focus on the Eastern Europe-Central Asia region and the second was held in Kuala Lumpur, Malaysia (December 2010), with a focus on the Asian region.

This meeting report summarizes the discussions and recommendations from the consultation held in Buenos Aires.

INTRODUCTION

Between 2001 and 2009, HIV incidence globally fell by more than 25% in 33 countries. While this is a very significant achievement, it is important to know that during that same period, HIV incidence increased by more than 25% in five Eastern European and Central Asian countries. A significant number of these new infections occurred in people who inject drugs.[1] In the South-East Asia region, estimates show that in some countries, 40% of people who inject drugs are living with HIV.[2] In parts of the Latin American-Caribbean region, high rates of HIV transmission continue to occur among networks of people who inject drugs and their sexual partners.[3] In Central and South America it is estimated that as many as 2 million people inject drugs and that more than one quarter of those might be living with HIV.[4]

Providing people who inject drugs with proven HIV prevention methods not only contributes towards their human right to health, but it is also a public health imperative. To ensure that prevention methods are safe, efficacious, and accessible for this population, novel prevention strategies and approaches must be assessed from this community's standpoint and, for this reason, people who inject drugs must participate in HIV preventive research.

Meaningfully engaging people who inject drugs in HIV prevention trials, however, poses challenges that require specific ethical considerations and guidance. These challenges include, but are not limited to: stigma and discrimination; criminalisation of people who use drugs; harsh policing practices; illegality or inaccessibility of sterile injecting equipment, opioid substitution therapy, and overdose rescue medication; the prevalence of comorbidities such as viral hepatitis, tuberculosis, and mental health illness; as well as lack of access to basic services such as health care and supportive housing options; high unemployment rates; and too often, an overall lack of respect for the basic human rights of people who inject drugs.

In light of these challenges, UNAIDS and WHO, through their joint HIV Vaccine Initiative (HVI), embarked upon a series of regional key stakeholder consultations aimed at developing a guidance point specific to the engagement of people who inject drugs in HIV prevention trials. In order to ensure that those closest to the front-line of these issues had an opportunity to share their experience and knowledge, participants at each of the consultations included researchers, ethicists, and activists, some of whom are from networks of people who use drugs. The first consultation was held in Istanbul with a focus on the Eastern Europe-Central Asia region (June 2010). The second consultation discussed the challenges being faced in the Asian region and was held in conjunction with the *Lancet* special series symposium on "HIV in people who use drugs" in Kuala Lumpur (December 2010). This report is based on the outcomes of the third consultation, held in Buenos Aires with a focus on the Latin America-Caribbean region (April 2011). At each of the three consultations, participants were asked to consider specific regional challenges - legal, regulatory, structural, social and logistical - to involving people who inject drugs in biomedical HIV prevention research and strategies that could overcome these.

The Buenos Aires consultation was characterized by lively, interactive, and informed discussions. Participants provided evidence of two trends among people who use drugs in the region. First, it was noted that there was an overall decrease in HIV incidence among people who inject drugs largely attributable to safer injecting practices resulting from prevention campaigns, harm reduction programmes, and access to antiretroviral treatment.[5] Second, drug injecting is declining in favour of intranasal drug administration routes (snorting, sniffing and

[1] UNAIDS Report on the global AIDS epidemic 2010, p. 8.
[2] UNAIDS, AIDSinfo 2010.
[3] *Ibid*., p. 17.
[4] *Ibid*, p. 46.
[5] Rodríguez, C.M., Marques, L.F. and Touze, G. (2002) "HIV and injection drug use in Latin America", *Aids*;16 Suppl 3:S34-41.

smoking). There has been a transition towards use of crack cocaine and other cocaine derivatives, such as "pasta base/free base", "oxi"[6] glue, and ketamines,[7] which are less expensive, have a faster effect than injected drugs, and usually very toxic. Studies show that people who smoke crack have higher HIV prevalence than that among people who inject drugs,[8] which could be explained by increased unsafe sexual practices precipitated by the use of crack.[9] HIV prevalence among intranasal cocaine users and smokers was found to be 6.3% in Buenos Aires, 9.5% in Montevideo and 7.9% in Santa Lucia,[10] compared to 5% HIV prevalence among people who inject drugs in Brazil.[11] While injecting drugs with potentially contaminated equipment increases the risk of HIV acquisition, use of drugs that are not injected can place people at higher risk of HIV exposure.[12]

In many Latin American cities, HIV prevalence is higher among people who inject drugs than in the general population.[13] That said, according to the Pan-American Health Organization (PAHO), both people who inject drugs and people who use non-injected drugs are considered as populations at higher risk of HIV exposure, with a combined HIV prevalence that is about 10 times higher than in the general population in the region.[14] Additionally, people who use non-injected drugs face challenges similar to those experienced by people who inject drugs. Poverty, low levels of education, gender discrimination, overt street-level police action and over-policing, and homelessness or unstable housing environments are all factors that contribute to the vulnerability of people who use drugs.[15]

In the light of these considerations, participants in the Buenos Aires consultation agreed that the ethical and scientific considerations for involving people who inject drugs in biomedical HIV prevention trials should apply to all people who use drugs, since these practices place them at higher risk of acquiring HIV. They recommended that the original wording of the title "People who inject drugs: guidance for their ethical engagement and meaningful participation in biomedical HIV trials" and text of the guidance point should be changed in order to reflect this consideration. Accordingly, the text of this report further on will refer to people who use drugs in general, and will only distinguish between people who

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[6] This is a Brazilian crack-cocaine formula, in which cocaine is used with querosene and/or battery acid, especially used at the Amazon region.

[7] Inchaurraga, S. (2003) "Drug use, harm reduction and health policies in Argentina," *Clinical Infectious Diseases,* vol 37 supl 5, p 376 – 372.

[8] Edlin, B.R. *et al*. (1994) "Intersecting epidemics – crack cocaine use and HIV infection among inner-city young adults", *New England Journal of Medicine, 331*, 1422-1427; Word, C.O. and Bowser, B. (1997) "Background to crack cocaine addiction and HIV high-risk behavior: The next epidemic", *American Journal of Drug and Alcohol Abuse, 23*, 67-77, cited in Day, M., *et al* (2004) "Risk Behaviours and Healthcare Needs of Homeless Drug Users in Saint Lucia and Trinidad", *The ABNF Journal*, available at: http://findarticles.com/p/articles/mi_m0MJT/is_6_15/ai_n8592430/

[9] Castilla, J. *et al*. (1999) "Drug and alcohol consumption and sexual risk behavior among young adults: Results from a national survey", *Drug & Alcohol Dependence* 56, 47-53, cited in Day, M., *et al* (2004) "Risk Behaviours and Healthcare Needs of Homeless Drug Users in Saint Lucia and Trinidad", *The ABNF Journal*, available at: http://findarticles.com/p/articles/mi_m0MJT/is_6_15/ai_n8592430/

[10] *Ibid*.

[11] Ralón, G. *et al.* (2008) "Vulnerability associated with HIV transmission among drug users in three countries in South America: Argentina, Brazil, and Uruguay (1998-2004)," *XVII International AIDS Conference* (August 3-8, 2008). *Abstract Book*, Volume I, pp. 145-146, Mexico City.

[12] One review article focused on Brazil reported that people who inject drugs had a seven-fold increase in their risk to be HIV-infected, when compared to non-injection drug users. However, injection drug use in Brazil has been declining in recent years. Recently published studies tend to recruit larger samples of crack cocaine and/or snorted cocaine users rather than people who inject drugs. Malta M, *et al.* (2010) "HIV prevalence among female sex workers, drug users and men who have sex with men in Brazil: a systematic review and meta-analysis", *BMC Public Health*, 7;10:317.

[13] In particular, Porto Alegre, Itají, Sáo José do Río Preto, Sáo Paulo, Apta, Sorocaba, Rio de Janeiro, Salvador, Florianópolis, Porto Alegre and Gravatí (Brazil), Buenos Aires and Great Buenos Aires (Argentina), Asunción and suburban cities (Paraguay) and Montevideo (Uruguay). Rossi, D. (2009) "VIH en Personas que Usan Drogas en América Latina y el Caribe", in *Retos planteados por la epidemia del VIH en América Latina y el Caribe*, Chapter 2, ONUSIDA /UNICEF/OPS-WHO.

[14] Ralón, G. *et al.* (2007) "Vulnerabilidad asociada a la transmisión de VIH entre usuarios de drogas del Área Metropolitana de Buenos Aires y ocho ciudades de Brasil (1998-2004)". *VII Jornadas de Debate Interdisciplinario en Salud y Población*, Instituto de Investigaciones Gino Germani, Facultad de Ciencias Sociales (UBA). August 8-10, 2007. Buenos Aires.

[15] UNAIDS Istanbul Background Document, p. 8.

inject drugs and people who use non-injected drugs when this distinction is especially pertinent.

The report has four sections. The first presents general considerations regarding several guidance points from the UNAIDS/WHO *Ethical considerations in biomedical HIV prevention trials* guidance document that have direct relevance for the topic of this consultation. The other three sections focus on the following themes discussed in breakout groups: (1) concerns related to vulnerability; (2) special considerations related, to conducting research in closed settings such as prisons, treatment centres, and other forms of detention; and, (3) discussion of challenges and strategies that acknowledge and address other comorbidities, such as tuberculosis, hepatitis, and mental health illness. Participants recommended that the new guidance point under development should further expand upon the existing guidance points, some of which may themselves need to be amended by adding new commentaries.

PART I GENERAL CONSIDERATIONS

Community participation in early phases of research

The existing *Ethical considerations* and *Good participatory practices* guidance documents recommend that research populations participate in a meaningful way in each stage of a trial, including the earliest stages during which a study is conceptualized and research protocols are developed. In previous consultations, participants suggested that increased community participation would lead to better research designs, both because protocols would be more sensitive to the needs of affected populations and because the trust that is developed by working closely together in the very early stages of research could facilitate access to and engagement of these often hidden, hard-to-reach populations.

At the Buenos Aires consultation, an additional benefit was recognized. It was pointed out that community involvement could also help to set research agendas by aligning research objectives with a community's interests and concerns, and by suggesting additional objectives relevant from the community point of view that might not have been considered otherwise as primary objectives.

Community advisory boards

Participants discussed community involvement primarily in terms of participation on Community Advisory Boards (CABs). Experience with CABs has generally been positive in the region, however some difficulties have been encountered in their formal establishment and functioning. Examples of these difficulties, or 'stumbling blocks', include the lack of clear delineation between a CAB's functions and responsibilities and those more properly belonging to ethics committees and lack of clear and agreed-upon criteria for membership on a CAB. Procedures for renewal and rotation of CAB membership must ensure that adequate community representation and a transparent relationship with the community are preserved. An additional concern expressed was how to ensure that new CAB members maintain their objectivity vis-à-vis the broad goals of the research and are not seeking membership in order to interfere with the research objectives, motivated by a predisposed bias against the research. Participants suggested that, in order to avoid future problems in the creation and organization of CABs, the UNAIDS/AVAC *Good participatory practice guidelines* (GPP) should provide a clear definition of a CAB's objectives, its role, and responsibilities. Suggestions of relevant procedures for CAB establishment and functioning would help ensure transparent and effective input from community stakeholders, based on real perspectives and needs.

Networks and organisations of people who inject drugs

The Peruvian site of the multi-site iPrEx pre-exposure prophylaxis (PrEP) trial, which enrolled men and transgender women who have sex with men, was cited as a successful example of community participation, due in part to a pre-existing high level of organisation and communication within the MSM communities. These communities are largely aware of their rights and needs, and have a strong history of activism and advocacy that stands in sharp contrast to the experience of people who use drugs. Indeed, doubts were expressed about the feasibility of creating networks of people who use drugs given the regional particularities of this population. In Latin America, as elsewhere, the fight for access to opioid substitution therapy (OST) or needle and syringe programmes (NSP) has been an opportunity for people who inject drugs to form networks and work together for their rights. However, with injecting drug use declining in Latin America and the Caribbean, and other drugs and routes of transmission on the rise, there is no common cause to unite people who use non-injected drugs. There is, for example, no equivalent substitution therapy for users of crack cocaine and other cocaine derivatives. Consequently, people who use non-injected drugs in Latin America and the Caribbean lack the same incentives to form networks and advocacy organizations. Additionally, cocaine use triggers a self-centred form of behaviour and drug consumption. People who use cocaine may not gather for social consumption of the drug which inhibits the development of social networks among people who use cocaine. Finally, the stigma related to drug use, and especially crack use, prevents people who use drugs from publicly presenting themselves as such. Their drug use is both criminalised and subject to social discrimination. Even in countries where possession of drugs for personal use is not punished by law (as, for example, in Uruguay or Mexico), drug use is still stigmatized and socially rejected.[16] Participants noted that people who disclose their drug use might lose their jobs, be exposed to police violence, and can even be marginalized by drug dealers and other people who use drugs.[17]

Involvement of local authorities in the research

Guidance point 2 in the *Ethical considerations* guidance document recommends that the selection of the community for consultation and partnership should be discussed with relevant local authorities.

> *Defining the relevant community for consultation and partnership is a complex and evolving process that should be discussed with relevant local authorities. As more groups and people define themselves as part of the interested community, the concept needs to be broadened to civil society so as to include advocates, media, human rights organizations, national institutions and governments, as well as researchers and community representatives from the trial site. Partnership agreements should include a clear delineation of roles for all stakeholders and should specify the responsibilities of sponsors, governments, community, advocacy organizations, and media, as well as researchers and research staff.*[18]

Questions were raised about which authorities should be consulted regarding research with people who use drugs, how to involve authorities when they can

[16] Inchaurraga, S. (2009) *Human rights and drug use Handbook – Manual sobre Derechos Humanos y Uso de drogas*, Rosario, CEADS UNR.

[17] The Ombudsman's Office in Buenos Aires reported that 80% of the more than 3500 people who are seeking treatment for drug use are unemployed and 65% have not finished secondary school. In January, the city major vetoed a law that would have created an employment programme for this population. "La Defensoría porteña alerta sobre la exclusión a adictos en recuperación", *Tiempo Argentino,* 26 May, 2011. News report available at: http://tiempo.elargentino.com/notas/defensoria-portena-alerta-sobre-exclusion-adictos-recuperacion

[18] UNAIDS and WHO. Ethical considerations in biomedical HIV prevention trials. Geneva: UNAIDS, 2007.

imperil participant well-being, and the role of authorities in the recruitment of participants.

a) Relevant authorities

Participants identified a number of public authorities and officials who potentially could be consulted regarding upcoming research. These included public health authorities, officials in the legal and judiciary system, local decision makers, prison functionaries, and staff of emergency services and health institutions. However, public officials and governmental authorities were specifically excluded for several reasons. In most countries, drug use is not considered a public health priority and there is a perception that public officials lack knowledge about, and concern for, people who use drugs, resulting in little or no interest in providing them with appropriate services.

Moreover, since criminalisation of drug use is common across the region, the question of how to effectively engage authorities in ways that would not compromise the research was addressed. One participant suggested that contact with authorities should follow a bottom-up strategy: contact with the relevant authorities should only be established after consulting with community representatives, networks of people who use drugs, and other non-governmental organizations (NGOs) as to whether involving the authorities might compromise the well-being of research participants.

One of the consequences of not engaging authorities from the outset in an early and transparent process, however, is that opposition from the authorities to a trial that is already underway, could seriously hinder the continuity of the research. This consideration also serves to help define who should be considered an 'authority'. One participant defined authorities as those public officials who have the authority and power to hinder or facilitate research.

To address these concerns, it was agreed that context is highly relevant in deciding which authorities should be contacted and in what manner. There are countries in which people who use drugs are included in, or represented by, some public agencies, such as Argentina's National Institute against Discrimination, Xenophobia and Racism (INADI). Some participants also reported good communication with prison authorities and health teams in Mexico and Peru.

b.) Transparency

Participants cited transparency as an important concern when involving public authorities in a study. It was noted that providing full information about the objectives of some trials to authorities could both imperil research participants and hinder research. In one study conducted in prison facilities in Argentina,[19] the study's objectives were disguised in order that researchers could provide informational material and equipment for sterilizing injecting equipment. Prison authorities were told that researchers were going to conduct workshops about tattooing, which, although not allowed in prison settings, is more easily accepted by authorities than drug injecting.[20] Questions were raised about the

[19] ONUSIDA (2003) *Cárceles y HIH/SIDA Avances en la prevención y en el mejoramiento de la asistencia en VIH/SIDA en cárceles de Argentina.*

[20] The Project "*Prevention and Support on HIV/AIDS to adult persons in prisons*" was developed in 2003 in twelve Argentinean units with the aid of UNAIDS funds. The project, conducted by the Drug Abuse and AIDS Advanced Studies Center (CEADS) of the National University of Rosario in Male's Unit 3 in Rosario city, was the only one offering harm reduction modalities related to drug use. Such activities included workshops on disinfecting techniques, the training of peer educators on safe use, and the provision of information about drugs and preservatives. ONUSIDA (2003) *Cárceles y HIH/SIDA Avances en la prevención y en el mejoramiento de la asistencia en VIH/SIDA en cárceles de Argentina*. Buenos Aires, P. 25: 43

extent of transparency, and it was agreed that transparency should not override concerns about privacy and confidentiality.

Recruitment of participants

The most important challenges in recruiting people who use drugs derive from the criminalisation of drug use – and the people who use drugs - and the stigma that accompanies this practice. People who use drugs are, therefore, an understandably 'hidden population'. Because people who use drugs are highly vulnerable, the effort to contact them for research purposes poses a number of questions concerning privacy and confidentiality. Although these questions and concerns are common to all research, they are particularly pressing when considering the risks that can follow from not addressing sensitive issues related to recruitment of people who use drugs. Will participants be publicly identified as people who use drugs because of their relation to the study? Will they have to face any problems with the authorities (police and judicial system, child welfare, social services) because of their involvement in a trial?

Despite their vulnerable status, participants noted that in many cases, research protocols do not generally explain in adequate detail how the recruitment process will take place, including:

- how potential participants will be identified
- where participant recruitment will take place
- how the recruitment process will be conducted in order to protect the privacy of this population.

Participants pointed out that these processes are context-dependent. Regional harm reduction experiences in economically poor settings have shown that access to marginal areas where people who use illicit drugs live or meet is only possible with the help 'facilitators' from that same community, for example, other people who use drugs or trusted others.[21] It was agreed that governmental organizations might not be the best medium through which to contact people who use drugs; the best option would be civil society organizations and the key informants –individuals from local communities who also use drugs.[22] Their role is to facilitate entrance into settings such as shanty towns and marginalised neighbourhoods that can be difficult for researchers to access.

Apart from criminality, participants agreed that other social and economic factors that often influence the voluntariness of trial participation, do not, in general, differ from problems posed for other key populations that are similarly vulnerable.

Women

It was widely agreed that women who use drugs should be included in HIV prevention trials as per Guidance point 9. Regarding the inclusion of non-pregnant women, no further suggestions were put forth that would add to the existing guidelines. However, the conditions under which pregnant women should be included in prevention studies were much discussed.

Pregnant women

In practice, women who become pregnant are discontinued from biomedical HIV prevention trials. Although the Ethical Considerations GP 9 seems to suggest that women should stay in a study even if they become pregnant, it does not

[21] Inchaurraga, S; Siri, P. (1999) *First steps in assessing intravenous drug use with RAR at Rosario city*, International Journal on Drug Policy, IJDP. Inchaurraga, S. *et al*. (2002). *Drogas; haciendo posible lo imposible, Reducción de daños en Argentina - Drugs, making possible the impossible. Harm reduction in Argentina*, Rosario, CEADS – UNR.

[22] One participant used the term "abrepuertas" or "door openers" to refer to key informants. However, during the consultation, a community representative voiced her uneasiness with the concept of "abrepuerta", pointing out that doors are open and that no facilitators are, in principle, needed. However, since experience has shown that researchers and public officers have only a transitory interest in the prioritised communities, these communities have become more reticent and distrustful of projects that do not offer any permanent solutions to their needs.

explicitly consider this issue. Like other people who use drugs, pregnant women who use drugs are at higher risk of HIV exposure, acquisition, and transmission. There was an agreement that they should be included in research and benefit from its outcomes. Participants of the consultation pointed out, however, that precautions should be taken. Pregnant or breastfeeding women who use drugs should not be included in a trial until there is reason to believe that there is specified degree of safety established in the use of the approach in question in this population. Generally, as is the case for children, research should be at an advanced stage before this group is included in a trial.

A current study at the University of Rosario[23] focuses on the effects of medical prejudices about women who use drugs and become pregnant. The study was motivated by the fact that several women who used drugs and tested negative for HIV at the beginning of their pregnancies seroconverted at some point during their pregnancies. Their seroconversions passed undetected by their physicians, likely because drug use and HIV acquisition during pregnancy are taboo subjects that are seldom discussed among doctors and their pregnant patients.[24]

One participant expressed concern that restrictions on the participation of pregnant women who use drugs in research are based on a concern for the well-being of the foetus rather than concern for the woman. However, since most Latin American and Caribbean countries have laws that heavily restrict and criminalize the provision of therapeutic abortion, concern for the foetus does not necessarily involve an ethical commitment to its moral status, but rather, the recognition that the foetus will most probably become a person whose future interests could be negatively affected by the woman's inclusion in a trial. Restricting the participation of women in research acknowledges the possibility of affecting the interests of the people who will be born in the future to pregnant women participating in research, but it does not accord the foetus special status.[25]

One participant suggested that the final decision about inclusion of pregnant women should rely on the evaluation of an ethics committee, and that the decision of whether the inclusion is safe for the woman and the foetus should be made taking into consideration the kind of study and state-of-the art knowledge concerning safety of the product being tested. However, another participant pointed out that this procedural solution is not entirely satisfactory as it avoids the core ethical question. Because considerations about the well-being of a woman and a foetus are part of ethics evaluation, ethics committees might make divergent decisions about the inclusion of pregnant women in a trial. The guidance being developed through this process may be of assistance in this instance.

Children and adolescents

According to Ethical Considerations GP 10, children and adolescents should be included in clinical trials for prevention HIV methods. In the case of children and adolescents who use drugs, a problem arises when parents are not aware of their child's drug use. Should parents be asked to give their permission for involving a minor in research? It was suggested that children and adolescents

[23] CEADS UNR (2010) *Prevention Programme of HIV vertical transmisión and Harm Reduction with Mothers that use drugs - Programa de Prevención de la transmisión vertical del VIH y Reducción de daños en madres usuarias de drogas*. Memorandum not published. CEADS, National University of Rosario.

[24] Although these cases are rare in numbers, they illustrate a gender bias in medical professionals that should be taken into consideration.

[25] See Parfit, D. (1976) "Rights, Interests and Possible People", in S. Gorovitz (ed.), *Moral Problems in Medicine*, Engelwood Cliffs: Prentice Hall, and Harris, J. (1992), *Wonderwoman and Superman, The Ethics of Human Biotechnology*, Oxford: Oxford University Press, for the philosophical background of this discussion.

should be asked whether their parents are aware of their drug use and whether they would allow their parents to be contacted in order to ask for their consent.

Another question regarding the enrolment of children and adolescents who use drugs concerned where recruitment should take place. Could this be in clinics for treatment of sexually transmitted infections; centres that offer voluntary HIV counselling and testing; and other locations such as schools, clubs, and recreational centres? In each of these cases, there is a possibility of stigmatising the relevant population by publicly revealing their higher risk of HIV exposure. One partial solution to these two problems would be to establish contact with the relevant population through drug treatment centres. Although not all legislation requires parental consent for drug *treatment* in these centres, the centres might nevertheless require parental consent for inclusion in research.

Availability of outcomes

In general, participants at the consultation agreed that vulnerable populations should have access to any successful outcomes at the conclusion of trials. It was acknowledged that some populations, such as children and infants, will have public support assuring access to research outcomes, while other populations, including people who use drugs, might be denied public funding due to social stigma and lack of interest in their general well-being and right to health care. One participant put forward the idea that international guidelines that regulate research would support a claim that *all* research subjects acquire a certain layer of vulnerability by virtue of participation in a trial and that this entitles them to have access to the outcomes of research.[26]

Who should be responsible for providing access to the studied approaches once a successful trial is over? Researchers, sponsors, and local governments were proposed as possible candidates and participants agreed that there should be mechanisms to prevent “safari” or “parachute” research, i.e. research that has no relation to the communities’ needs and leaves no benefit after the trial is completed. Guidance point 19 in the Ethical Considerations guidance currently deals with this issue and nothing more was added.

In Brazil, the National Committee of Research Ethics has argued that it is an obligation of the sponsor to ensure participant access to the results of research when the research products are better than the standard treatment offered locally.[27] Another obligation for sponsors is that new drugs approved as a result of the trial must become available in the country. If a new drug is tested in Brazil, it must become available in the market after trial completion. This, however, does not mean that the sponsor’s obligation to provide the drug to the research participants ceases. Sponsors are not released of their obligation towards research participants until the government provides the intervention to the general population.[28]

[26] World Medical Association (2008) *Declaration of Helsinki*, specially articles 14 and 33.
[27] Citation needed.
[28] Although this assures that no trial participant will cease to receive the outcomes of research, concern was raised about the strategy that some pharmaceutical companies have displayed in order terminate their obligations. It was mentioned that drug companies are supporting trials with the hope that courts will order the government to provide the new tool to the general public should it prove effective. (Procuradoria ataca laboratório em defesa contra ação judicial15/07 -12:38 -Agência Estado).

PART II VULNERABLE POPULATIONS

The concept of vulnerability

At several points in time during the consultation, concern was expressed as to whether and why people who use drugs should be treated as a vulnerable population. For this reason an approach based on different "layers of vulnerability"[29] was favoured for analyzing and addressing the vulnerabilities of people who use drugs in a structured fashion.

According to the layers approach, vulnerability is not a unified characteristic that applies to all potentially vulnerable populations or individuals. Numerous factors render people vulnerable and it is these factors - and the interaction between them - that forms what can be conceptualized as 'layers' which are indicative of the degree and extent of vulnerability. Thus, a transgender person, of colour, who uses drugs, sells sexual services, and is HIV-positive, will have several 'vulnerability layers', each of which should be considered in order to address her/his particular needs. This person may be vulnerable to discrimination because of his/her transgender status and may be additionally vulnerable (have another layer of vulnerability) to violence, for example, in a prison setting because they have previously sold sex. Vulnerability is, then, not an internal characteristic but, rather, is dependent upon the context. A woman may not be particularly vulnerable in a society in which she has equal power and opportunity to men, for example.

These different layers should be distinguished in order to understand the factors and their interaction in contributing to vulnerability, and in order that researchers and health providers might act accordingly, including developing specific safeguards to protect participants from risk. For example, because there are laws and regulations which contribute to the vulnerability of people who use drugs - their drug use is criminalised - extra caution must be taken to ensure confidentiality. Other vulnerability layers include cognitive and psychiatric conditions that, when occurring with drug use, can reduce autonomy and compromise capacity for decision-making. Common issues that compound vulnerability include poverty, social stigma, lack of access to appropriate health care, and discrimination due to gender, race, and ethnicity.

People who use drugs are not, of course, a homogenous group and participants pointed out that *not* acknowledging differences among, for example, patterns of drug use (dependent/addictive versus occasional) can actually generate further layers of vulnerability. In circumstances in which the health system discriminates against people who use drugs, and only identifies drug use with addictive behaviour, non-addictive drug behaviour is often overlooked by medical teams. Because there are potential adverse drug interactions between recreational non-prescription drugs and antiretroviral drugs, it is important that people feel free to discuss their occasional drug use – as well as any use which is more than occasional - with their HIV care provider.

It was recommended that researchers be aware of the many layers of vulnerability which affect a given population, and that special attention be paid to those layers that threaten the confidentiality of research participants.

Addressing layers of vulnerability

The question was raised as to whether research protocols must explicitly identify each vulnerability layer and how the research will address it so as to not put the research participant at risk. Participants agreed that although some issues should be explicitly addressed in the protocol, (i.e. considerations regarding the potential loss to follow up of participants due to violence and incarceration, and the way in which participants will be contacted if they become incarcerated), it was noted that if researchers are sufficiently familiar with the vulnerability of a

[29] Luna, Florencia. "Elucidating the Concept of Vulnerability: Layers Not Labels." *International Journal of Feminist Approaches to Bioethics* 2.1 (2009): 121-139.

given population and the ethical implications of such a vulnerability, they will design more sensitive protocols. The suggestion was made that researchers receive more education in bioethics and human rights as a way of sensitizing them to the issues and to possible ways of mitigating risks.

While researchers are responsible for addressing the vulnerabilities of a given research population, they are not alone in doing so. Research ethics committees and community advisory boards—and other types of community engagement mechanisms—should be aware of, and sensitive to, the multiple and complex ways that people who use drugs can be vulnerable. They should not be excluded from research because of a misguided belief that they will be unduly put at risk and should not be denied cash remuneration for fear that they will spend it on drugs. It was noted that this emphasis on the important role of ethics committees reinforces the significance of local resources capable of conducting ethical and scientific review because only they could know and assess the particularities of the local context.

Informed consent

Because of the multiple layers of vulnerability that can affect people who use drugs, it was recommended that special attention should be paid to the informed consent process in order to make sure that participants completely understand the implications of being involved in research. This may be particularly challenging given the high rates of illiteracy in the region.

Participants explicitly considered recommendation 2.10 in the Istanbul report, which states:

> Within the informed consent process, researchers should disclose all the known risks of participation, including legal and regulatory requirements to declare infectious diseases to public health authorities or report child abuse, sexual violence, or other intimate partner violence to police authorities. This may include notification of sexual partners and of peers who may have used contaminated injecting equipment after the participant, if testing positive for any sexually transmitted or blood-borne infection. Researchers should make clear any limits on their power to guarantee full protection of participants' confidentiality.[30]

During the informed consent process, researchers should also explicitly address with participants the legal risks related to drug use and drug trafficking. Even when this is not a risk exclusively related to trial participation, participants in the Buenos Aires consultation agreed that all risks related to reporting to a legal system should be differentiated and each addressed separately. Trial participants should, therefore, be informed about researchers' moral and legal obligations, which may include the requirement to report to relevant authorities, knowledge of infectious diseases, child abuse, or sexual violence. They should be reminded of the legal risks that they face not because of trial participation, but because of criminalisation of drug use.

Participants raised concerns about the possibility of researchers having to notify sexual partners about a trial participant's HIV status. Practical and ethical objections were raised. Who should be contacted when sexual partners are to be notified? The legal partner? Other partners? Is it morally admissible to breach confidentiality in favor of sexual partners? It was noted that recommendation 2.10 (above) addressed the fact that researchers might be constrained by legal regulations or moral imperatives, and that trial participants should be aware of these constraints. For example, in a country where there is no legal obligation to report child abuse, a researcher might nevertheless decide to report such abuse for moral reasons. In that case, trial participants should know in advance the way in which child abuse will be handled during the research trial. However, since participants were not clear whether disclosure to sexual partners should be done in the absence of regulations requiring it, or even in the face of such regulations,

[30] Istanbul Consultation Meeting Report.

one participant suggested that this particular case should not be listed in the EC document.

Remuneration issues

a.) Fair remuneration and voluntariness of participation

Although it was agreed that participants should be remunerated for their participation in research, and offered free transportation to and from the study site, several questions were raised about the amount and kind of remuneration that should be offered. There was a general concern that remuneration might influence the voluntariness of participation. The participants of the consultation agreed that the right amount of money could not be determined in general and without proper attention to the local context. In the end, ethics committees and CABs should have the last word in evaluating how adequate the remuneration is in relation to each particular setting, the characteristics of the trial, and the particular vulnerability layers of the community involved.

Concern was raised, however, regarding the possibility of arbitrary decisions and the use of dissimilar criteria in similar circumstances. It was noted that in the context of the same trial, the University of Sao Paulo does not allow for any kind of remuneration other than vouchers for travel to the research site. At the research site at the University of Rio de Janeiro, however, remuneration is allowed.

b.) Amount and type of remuneration

In order to avoid paternalistic attitudes towards people who use drugs, some participants suggested that the amount of remuneration should be calculated in the same way as it is for other research participants with similar incomes who take on equivalent burdens and time commitments. The contrary argument was also made: that the type of remuneration – cash or coupons for example - should change according to the specific drug use profile of the prioritised population as not all people who use drugs are similar in autonomy and decision-making capacity. Whether cash or other goods should be provided could, some argued, vary according to the type of drug used and level of addiction exhibited by a given participant. Thus, while cash remuneration might not be of great concern in the case of people who use drugs occasionally, it might be more controversial in the case of people who have a drug addiction. Furthermore, the type of remuneration should respond to the medical imperative of not harming the participants. This does not mean that some participants should be compensated more than others, but rather, that there are relevant differences among people who use drugs, which might justify providing cash remunerations in some cases and not in others. Concern was voiced with regard to the paternalistic character of this suggestion. However, the participants agreed that if different remuneration practices were proposed, the decision should be accepted by community members and by ethics committees.

c.) Methodological considerations

Close attention should be paid to remuneration not only because of the risk of inducing vulnerable populations to participate in a trial, but also for methodological reasons. In South Africa, it was decided at a national level to set a compensation for study participation equivalent to 2-3 weeks of salary. As a result, some of the trials had trouble with double enrolment. Some trial participants considered trial participation as a job and signed up for various trials, thereby compromising the results of each of the trials. When researchers learned of the practice, they had to exclude some of the trial participants from continuing in the trial with a significant impact on sample size. Although this is not an insurmountable problem, close attention should be paid to avoid

remunerations that are so high that they act as undue inducement to trial participation.

The possibility of offering different types of remuneration to trial participants raised doubts about data reliability. It was pointed out that if people who use drugs were offered different kinds of remuneration, research participants would quickly learn how to act in order to receive the preferred remuneration, thus invalidating the data obtained through their participation. One participant also pointed out that, in some cases, the remuneration offered to key informants or community facilitators had been problematic. Since they were in financial need themselves, the facilitators did relax inclusion criteria, trying to recruit as many people as possible and putting their own interests above the research objectives.

Gender

Gender was considered as another additional way in which a population's vulnerability was not adequately represented in the existing guidelines. Although there is a guidance point (Ethical Considerations GP 9) dedicated to women and different gender identities are mentioned throughout the document, it was suggested that a general category entitled "Gender" should be added and subdivided into several subcategories, addressing the ways in which other gender identities (transgender, for example) may increase a person's vulnerability.

Race and ethnicity

It was suggested that race should be considered among the vulnerability layers that are important in the region, even more so because race bias is seldom considered to be a problem in Latin American countries and usually goes unrecognized. Ignoring race identity issues not only makes race bias invisible, but it results in omission of relevant information that should be included in analyses in order to identify specific health issues in certain groups.

The discussion group on vulnerability pointed out that ethnicity, rather than race, is a more suitable category to understand bias and vulnerability in Latin American countries. It was stated that "race" refers to genetically determined differences, and is not applicable to indigenous populations. There was no clear agreement on this issue.

PART III RESEARCH IN CLOSED SETTINGS

General considerations

Research in compulsory drug detention centres (CDDCs) was a major concern in the Kuala Lumpur consultation. CDDCs, however, are a local phenomenon without equivalents in Latin America and the Caribbean. In this region, research in closed settings may concern prisons, voluntary treatment centres, and treatment centres inside prisons.

Although CDDCs have no parallel in Latin America and the Caribbean, the possibility of conducting ethical research in this context was still considered and found to be unacceptable. One participant pointed out that there is a necessary paradox involved in conducting research with people who use drugs in such settings because: 1) either the person (potential research participant) complies with the rules of the institution and no longer uses drugs, or 2) the person does not comply with the rules of the institution and continues to use drugs. In the former case, people are at no risk related to drug use and are therefore ineligible for a trial focusing on people who are at increased HIV risk due to the use of drugs. In the latter, trial participation would expose the person's infraction to the

authorities of the institution, thereby compromising his/her privacy and overall well-being.

It was also noted that the humanitarian principles proposed in the Kuala Lumpur consultation to govern and restrict research in CDDCs are difficult, if not impossible, to meet in any closed setting, whether they are detention centres, prisons, or voluntary therapeutic centres. Among other requirements, the Kuala Lumpur consultation recommendations state that in order to conduct research in CDDCs, researchers must have 'unimpeded access' to detainees without advance notice to authorities, authorities must guarantee that no data about the individuals will be shared, that participants' confidentiality will be respected, and that researchers must be satisfied that neither participation nor refusal to participate in the research will negatively affect the persons involved.[31]

Participants emphasized the fact that unimpeded access is never really feasible in prisons where safety is a major concern. Visitors must be announced to authorities and the participants must be brought to the researcher. There are several controls before and after contact is made with the person in a closed setting and restrictions apply for what can be taken into and brought out of institutions. Because of these realities, the researcher might be subjected to security searches, and there is no guarantee that the confidentiality of the research data obtained during interviews will be kept. Even voluntary treatment centres have rules that must be followed in order to meet with those who are taking part in the programme.

On the other hand, degrading and humiliating treatment seem to be present in many, if not most, closed settings.[32] According to participants, even voluntary treatment centres hold people against their will, sometimes without any legal due process and by the mere request of a family member.[33] The use of coercive and unscientific methods of treatment, including subtle violence and degrading treatment, is not uncommon.[34]

Finally, issues regarding privacy and voluntariness of participation were discussed. If the institution supports the research and has an interest in being involved, prisoners/clients might be pressed, in more or less subtle ways, to either enter or continue participation in a study. Furthermore, under these highly controlled conditions, mere participation in a trial can expose vulnerable persons to discrimination and stigmatization.

Participants of the Buenos Aires consultation agreed that research should be avoided in closed settings in general since there is no biomedical prevention method that seems to apply specifically to people who use drugs in closed settings and that could not be studied in other populations. This implies both that research should not start in these contexts and that participants should be discontinued from the research when entering reclusion. Arrangements should be made, however, in the case that a research participant enters prison or a treatment centre during the period of the research, in order to ensure an ethical process to discontinue his/her participation in the trial whether permanently or simply during the incarceration period.

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[31] Kuala Lumpur Consultation Meeting Report.

[32] "El Borda eliminó un servicio para adictos", *Pagina 12*, 27 April, 2011. News report available at: http://www.pagina12.com.ar/diario/sociedad/3-167079-2011-04-27.html

[33] "INADI Chubut, contra la persecución a los consumidores de marijuana", *El Patagónico,* 16 May, 2011. News report available at http://www.elpatagonico.net/index.php?item=nota&idn=98190&ref=hoy;

[34] Some examples of coercive, unscientific and degrading treatment that were mentioned in the consultation are holding people against their wish by the sole request of family members, using these centres for "curing" homosexuality as well as drug addictions, and sitting detainees on pots of chilli. In Ecuador, several cases have been brought to court asking to release people held in treatment centres against their will. These presentations report that people are held against their will in order to abandon drug use or change sexual behaviour, that they are denied all rights, and that they receive abusive and degrading treatment, being forced to take a sphincter relaxant, for example, and not cleaning their excretions.

Discontinuation of trial participation following incarceration

Because drug consumption is criminalised, people who use drugs are more likely to be incarcerated than other populations[35] or be placed in a closed setting for a variety of reasons.[36] In order not to compromise research, and in order to protect participants, special arrangements should be made with participants and authorities in the transition from one setting to another. Such arrangements should address the following:

- whether 'benefits' ought to be provided to trial participants who enter into closed settings, even if they are discontinued from the trial and, if so, what mechanisms need to be developed to allow this to happen
- whether, and under what conditions, participants will be reincorporated into the trial after their release
- whether, and how, participants should be contacted if they enter closed settings;
- what specific processes should be followed when discontinuing participants who enter into closed settings during their participation in a trial.

Access to research benefits during incarceration

Although it was recommended that research should not be conducted in closed settings, there was general consensus that participants should keep the benefits of trial participation when they are placed in a closed setting, to the extent that this is feasible. It must be noted that the term "benefits of trial participation" was broadly used to refer to harm reduction programmes[37] whose provision is mandated in research outside closed settings, such as access to sterile injecting equipment and condoms, and HIV testing and counselling. Although these would not strictly be considered as benefits of trial participation, one participant pointed out that, in countries where these approaches are not widely available for the general population they are regarded as an additional benefit by trial participants.

While it was agreed that such benefits should not be lost because of incarceration, this suggestion raised ethical and logistical concerns. On the one hand, access to certain prevention methods that are not accessible to others in the setting may result in reverse discrimination and a double standard among inmates. There is also a risk of stigmatizing the research population by signalling to other inmates and authorities that they are people who use drugs, people living with HIV, or people at higher risk of HIV exposure. On the other hand, it might be problematic to introduce condoms or sterile injecting material in contexts where sexual intercourse and drug use is widespread, although not allowed or even acknowledged by institutional authorities. The extent and weight of these concerns will vary according to each particular context, and researchers and sponsors should consider carefully whether it is feasible and ethically admissible that the benefits of the research be continued during reclusion.

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[35] The percentage of people who use drugs among prison populations varies according to country. In Mexico, drug related charges account for 9% of prision population, while the percentage rises to 36% In Ecuador, 30% in Bolivia, 23% in Peru, 19% in Brazil and 17% in Colombia. Transntional Institute (2011), *Al filo de la justicia. Leyes de drogas y cárceles en América Latina*, p. 11. See also, Inchaurraga, S. (2003) *Drogas, políticas prohibicionistas y daños / Drugs, Prohibitionist policies and harms in* Inchaurraga, S. (Ed.), *Las drogas entre el fracaso y los daños de la prohibición / Drugs between the failure and the harms of Prohibition.* Rosario, CEADS UNR /ARDA.

[36] Ranging from the voluntary search for treatment to the unvoluntary reclusion in a treatment center mandated by a court or a family member.

[37] There were major discussions during the High Level Meeting that took place in June 2011 in New York, concerning the differences between harm reduction and risk reduction. The two are not the same. Risk reduction often means teaching people to avoid risk behaviours and may include condom provision and syringe distribution or availability. However, risk reduction is only concerned with HIV transmission and acquisition and does not involve other drug use related harms such as drug overdose.

Rejoining the research trial following release

Since it was repeatedly stated that participants should be discontinued from research if they enter into closed settings, concerns were raised about further penalizing research participants by taking away the benefits of trial participation. One way of not excluding participants who enter closed settings from the benefits of research is to reintegrate them into the research trial post-release, in cases where that is possible. Researchers should explicitly consider in the protocol the circumstances in which participants can be re-incorporated into research. One such consideration, for example, would be the duration of the incarceration period. It was also noted that research participants may enter a closed setting in order to obtain treatment for drug dependence and it was suggested that change in drug use behaviour should not disqualify research participants from re-entering research after reclusion.

Scientific validity of data

Because of high rates of incarceration among people who use drugs,[38] there is a risk that the data collected by a trial might not be enough to reach significant conclusions or that the loss to follow up of participants might invalidate the trial's statistical power. On the one hand, the protocol should account for the possible loss of participants in calculating the number of people who must be enrolled in a trial to achieve adequate statistical power and, on the other hand, arrangements should be made to obtain information regarding participants who enter closed settings before they are discontinued from research. In the iPrEx trial in Peru, for example, arrangements were made with the prisons' medical staff in order to obtain a final blood sample from research participants and establish if seroconversion had occurred.

Although it was agreed that researchers should take efforts to arrange a final meeting with incarcerated research participants in order to obtain relevant data, important concerns about how to contact participants after detention has occurred will need to be considered.

Confidentiality and follow up

The likelihood of involuntary and voluntary incarceration (some people may choose to enter a closed facility) must be explicitly considered in the informed consent process and trial participants must be asked in advance whether the researcher may try to contact them if they miss appointments with the research team. If the participant agrees to be contacted, further information must be obtained about who the researcher may contact to learn about the participant's whereabouts and the kind of information that can be obtained regarding the situation of participants. One participant suggested that the community contact person or key informant would be a suitable person to provide information about participants without the need to contact family members and other persons with whom the participant might prefer not to disclose his/her drug use or imprisonment situation. Although this might be a suitable option, respect for privacy requires that the participant be asked and informed consent be provided before any inquiries are started. If the participant does not continue in the research trial when in the closed setting, researchers should re-establish contact with trial participants after they are released. This, of course, will require agreement and cooperation on the part of the trial participant.

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[38] INADI (2009) "Recomendacion general en materia de discriminacion a consumidores-as de drogas prohibidas", in Inchaurraga, S. (ed.) *Manual sobre Derechos Humanos y Uso de drogas*, Rosario, CEADS UNR

PART IV COMORBIDITIES IN PEOPLE WHO USE ILLICIT DRUGS

The mandate of the consultation was to provide input into the development of research ethics guidance for HIV prevention trials, primarily by discussing issues of importance to the Latin America-Caribbean region. Consequently, discussion was generally focused on trial participants who are HIV-negative. That said, in the Buenos Aires consultation, the discussion of comorbidities also included a discussion of issues experienced by people who use drugs and who test HIV-positive. This discussion provided important contributions towards a more specific ethical discussion of what is owed to trial participants who seroconvert during the course of the trial. What are their particular needs and are there additional ethical considerations and implications that should be considered for the guidance point?

General considerations

The widespread use of antiretroviral therapy (ART) has significantly increased life expectancy of people living with HIV. The ATHENA cohort study showed that at age 25 the expected life years remaining for asymptomatic HIV positive patients were 52.7, compared to 53.1 for the general population.[39] As life expectancy for people living with HIV approaches that of the general population, the causes of death have also changed. A study on causes of death among HIV infected adults in France between the years 2000 and 2005 showed that AIDS was responsible of approximately 30% of deaths.[40] Another major European study involving almost 40,000 HIV positive individuals on antiretroviral therapy showed that between 1996 and 2006, 50.5% of deaths were due to non-AIDS related causes.[41]

However, despite the fact that general prognosis of HIV-positive patients is increasingly similar to the prognosis of the general population, this is not the case for HIV-positive people who use drugs. Drug use affects HIV-positive patients in several ways:

- it delays diagnosis of HIV
- it complicates care because of overlapping signs and symptoms
- it is related to decreased retention in care and poor adherence to treatment
- poor adherence increases the risk of resistance to antiretroviral drugs
- HIV-positive people who use drugs have less access and respond less well to treatment. They face an increased rate of morbidity and mortality. In this population, mental illness, opportunistic infections, tuberculosis, and chronic hepatitis B and C are more common than among people living with HIV who do not use drugs.[42]

[39] van Sighem Gras L, *et al*. (2010) "Life expectancy of recently diagnosed asymptomatic HIV-infected patients approaches that of uninfected individuals", *17th Conference on Retroviruses and Opportunistic Infections*. February 16-19, 2010. San Francisco. Abstract 526.
[40] Lewden C, Mortality Working Group of COHERE (2010) "Time with CD4 cell count above 500 cells/mm3 allows HIV-infected men, but not women, to reach similar mortality rates to those of the general population: a seven-year analysis", *17th Conference on Retroviruses and Opportunistic Infections*; San Francisco, CA, USA; Feb 16—19, 2010. Abstract 527.
[41] Antiretroviral Therapy Cohort Collaboration (2010) "Causes of death in HIV-1-infected patients treated with antiretroviral therapy, 1996-2006: collaborative analysis of 13 HIV cohort studies", *Clin Infect Dis*. 2010;50:1387-1396.
[42] Altice F L, *et al*. (2010) "Treatment of medical, psychiatric, and substance-use comorbidities in people infected with HIV who use drugs", *The Lancet*, Volume 376, Issue 9738, Pages 367 - 387, 31 July 2010.

Importance of integrated care

Mental illness affects between 40 and 60% of people living with HIV who use drugs.[43] When working with people who use drugs, a triple diagnosis should be considered: HIV infection, drug use, and mental illness. The complexity of the clinical situation increases in relation to the other layers of vulnerability that affect this population.

Integrated care is fundamental for handling the complex situation of HIV-positive patients who use drugs. Suitably trained personnel should have experience with evidence-based approaches for treating drug use disorders and experience with HIV treatment, but should also be aware of how drug use, HIV exposure, ART, and drug treatment interventions might interact and affect each other. They should also have experience in psychiatric care and management of psychiatric patients.

There was wide agreement that there are practically no health teams in the region capable of offering an integrated approach towards HIV and drug use management. There are fewer than six integrated teams in Brazil. There are some private integrated teams in Rio de Janeiro, although the cost of treatment is high and the quality is doubtful. In Argentina, there are no integrated teams. There are some individuals that have wide experience in integrated treatment, but no teams have been specifically created in order to attend to issues specific to this population.

While participants agreed that integrated care should be promoted in the region, one participant anticipated resistance from health authorities to integrate medical practices. How could medical professionals be persuaded to offer integrated care to people who use drugs? Most existing services appeal to counselling as an alternative to integrated care. However, counselling, which has a limited and specific role, is part of integrated care, not a replacement for it. In response to this concern, one participant noted that the main obstacle for creating integrated teams was the model of medical care and education prevalent in the region, which emphasizes the role of the physician over other health care providers. It was suggested that experience acquired during the studies should help inform health resources and practices in order to contribute to local capacity building.

Research teams should be trained in order to be able to provide such integrated care. It was recommended that teams would include psychiatrists and/or psychologists and/or specialised nurses with previous experience in the management of substance misuse and different mental conditions.

Capacity building

In terms of capacity building, the suggestion was put forward that research centres ought to become models of care after research is concluded. In this way, the community would benefit regardless of the study's results. Another participant expressed concern regarding the terms in which such a requirement would be made, noting that if the guidelines establish the obligation to keep a research centre as a health facility after the study is conducted, many researchers and sponsors will be deterred from conducting research that could be potentially beneficial for the population concerned. An alternative would be to negotiate a transfer process prior to the commencement of the study.

It was agreed that at a minimum, in order to benefit the research population and contribute to capacity building, researchers should present relevant authorities

[43] 53% of opiate users, 38% of cocaine users and 35% of alcoholic suffer major depression, compared to 6% of the general population. Also, there is a three to 20-fold increase in antisocial personality disorder among chronic drug users (Roundsaville, B.J. (1991) "Psychiatric diagnoses of treatment-seeking cocaine abusers, *Archives of General Psychiatry*, 48(1): 43-51). According to the US Office of Applied Studies, between 20 and 33% of people who use illicit drugs had serious psychological distress during 2004. Data available at: http://oas.samhsa.gov/NSDUH/2k4nsduh/2k4tabs/Sect6peTabs1to81.htm#tab6.10b

with a report on how the research results and the experience gained during the study might inform improvement of local health care practice and public policies.

The Equatorian research site for the iPrEx study, the Fundación Ecuatoriana Equidad (Equatorian Foundation for Equity), is a community-based association that works for the rights of people who live with HIV, MSM, and the gay, lesbian, bisexual and transgender (GLBT) community. In order to act as a site for the iPrEx study, the Foundation created the Medical Institute for Research which conducted a treatment programme for MSM called "The Man's Clinic" (Clínica del Hombre). Much experience was gained concerning the treatment of sexual and reproductive health among gay and transgender people. Since the country did not have any public policies regarding sexual and reproductive health of MSM, this experience was valuable both in producing human resources and in informing public policies to address the sexual and reproductive health needs of MSM. After the trial ended, the research centre remained open to the public, and provided much-needed service to the community. Ecuador's Ministry of Health has incorporated this programme into its primary HIV services and is now working with the local research team to elaborate treatment guidelines for attending MSM. Additionally, the Medical Institute of Research is now one of the country's epidemiological surveillance centres for HIV and sexually transmitted infections among men who have sex with men.

Concern for voluntary participation

Because of the high rate of psychiatric comorbidities among people who use drugs, it was acknowledged that assessing the capacity of the potential participant to understand the informed consent process may be especially challenging. Cognitive disorders are associated with the long-term use of harmful substances, such as solvents and smokable cocaine. Psychiatric disorders may also result in biased and mistaken evaluations regarding trial participation. Thus, the level of understanding achieved should be assessed in the most comprehensive way possible in order to ensure that participation is really informed and voluntary. In case of acute intoxication, the informed consent process should be interrupted and enrollment postponed until the acute effects of substances that might distort judgment and perception are over.

Antisocial behaviour

It was also pointed out that, since psychiatric disorders can sometimes be linked to antisocial behaviour,[44] protocols should clearly and comprehensively define the procedures for dealing with participants who abuse or threaten the research team or other participants.

Treatment and care

A fundamental question regarding the involvement of people who use drugs in HIV prevention trials is the determination of what comorbidities should be treated and what level of care trial participants should be offered. Given that psychiatric disorders are among the most prevalent comorbidities among people who use drugs, they should be specially considered before and during the trial. Researchers should make plans for referral to specialized care, including full access to psychosocial and psychiatric care and attention to emergencies directly associated with the misuse of substances (e.g. overdose management) in addition to other contingencies. These should be defined before the implementation of the study and guaranteed over the entire course of the trial.

Participants suggested that HIV prevention trials should provide full access to care for medical conditions that may emerge during the study and that are

[44] Citation needed.

directly or indirectly related to the trial (e.g. a new infection in the context of a cohort study, the side effect of a medicine or vaccine, etc.). Researchers should be fully committed to use the best available resources, methods, and professionals as defined by the best practices available in each specific context. Depending on the nature of the protocol and respective interventions, it was accepted that treatment might be required after the trial is over. However, no specific recommendations were made and it was suggested that the extent of post-trial treatment should be determined and agreed upon by researchers, sponsors, ethics committees, public health authorities, and CABs.

Standard of prevention

Participants emphasized the need to implement activities aimed at reducing drug-related harms to research participants. This should include at least some of the interventions in the comprehensive package recommended in the WHO/UNODC/UNAIDS *Technical guide for countries to set targets for universal access to HIV prevention, care and treatment for injecting drug users*.[45] It was acknowledged, however, that many of these harm reduction and preventive interventions are not widely available in Latin American and Caribbean countries.[46]

Comprehensive package for the prevention, treatment and care of HIV among injecting drug users:[47]

1. Needle and syringe programmes
2. Drug dependence treatment (OST and other)
3. HIV testing and counselling
4. Antiretroviral therapy
5. Prevention and treatment of sexually transmitted infections
6. Condom programmes for people who inject drugs and their sexual partners
7. Targeted information, education, and communication for people who inject drugs and their sexual partners
8. Diagnosis and treatment of or vaccination for viral hepatitis
9. Prevention, diagnosis, and treatment of tuberculosis

Questions were also raised regarding other potential prevention modalities that are not included in this package and whose provision might be illegal. For instance, there is some evidence that marijuana can work as a substitution method for people who use crack cocaine and some cocaine derivates. However, its use and provision are criminalised in all Latin American and Caribbean countries. A participant noted that a pilot study conducted at the University of Sao Paulo reported that the use of marijuana in people using crack cocaine produced good substitution results.[48] Because of legal restrictions, the

[45] By PAHO's request, the Intercambios Civil Association, together with Marcus Day have adapted the WHO/UNODC/UNAIDS Technical guide to the Latin American And Caribbean region. This new document, "Guía Técnica Para establecer objetivos para el acceso universal a la prevención, tratamiento y atención del VIH para Usuarios de Drogas con Alto Riesgo de adquirir o transmitir VIH y otras ITSS", is currently being prepared for publication.
[46] Rossi, D. (2009), *op. cit*.
[47] WHO, UNODC and UNAIDS. *Technical guide for countries to set targets for universal access to HIV prevention, care and treatment for injecting drug users*. Geneva, 2009.
[48] In an interview, the chief researcher Dartiu Xavier states that 68% of participants completely abandoned the use of crack, and many abandoned the use of marijuana as well. *Carta Capital*, November 8th, 2010. Interview available at: http://www.teleios.com.br/2010/drogas-e-adolescencia-dartiu-xavier-entrevista/

researchers could not prescribe marijuana or openly advise participants to smoke it.[49]

It was suggested that the required harm reduction package should be in harmony with local legislation. However, discussion arose regarding the clause “in harmony with local legislation” that sometimes appears in international ethics guidelines. One participant pointed out that in cases in which internationally accepted harm reduction methods are criminalised and there are institutional barriers limiting access to adequate HIV prevention methods, harmonization may not be actually possible and might even be morally inadmissible.

Even if these legal restrictions can be negotiated with relevant authorities and an exemption obtained in order to conduct a trial, an additional issue must be considered regarding post-trial access to the outcomes of research when a proven harm reduction method involves the use of an illicit drug. The co-investigator of a heroin trial in Canada pointed out that the trial had shown that providing a small amount of the drug to people with heroin addiction reduced the disorder in their lives by improving their social interactions.[50] Since this was a state-sponsored trial, the provision of heroin during the trial had been allowed for trial purposes only. Ethical and legal challenges had to be faced when considering the possibility of making this proven harm reduction method available to the community of people who use heroin.

What should be required in the face of inappropriate local prevention standards? One participant argued that research in such conditions was morally unacceptable and should not be carried out at all. However, another participant responded that in some contexts, if the relevant community agreed to the research, measures could be taken to adapt the local facilities to provide internationally acceptable standards of prevention, even when these were not previously available. Participants agreed that harmonization with local regulations could sometimes be morally unacceptable and it was agreed therefore that the clause should not be included in the guidelines.

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[49] The use of cannabis could not be prescribed because a formal prescription would be illegal at that time in Brazil. The researchers requested a clearance in order to conduct a full trial, but did not receive such clearance.

[50] Wood W (personal communication).

CONCLUSION

The contributors to the Buenos Aires consultation agreed that it is imperative to acknowledge changes in the drug and HIV epidemics in the Latin America and Caribbean region and to engage all people whose illicit drug use places them at higher risk of acquiring HIV in biomedical HIV prevention trials. The guidance should be expanded beyond the initial focus on people who inject drugs.

While many participants emphasized the role of local ethics committees and community advisory boards (CABs) in protecting local populations, it was also recognized that an appeal to ethics committees and CABs only offers a procedural solution to substantial ethical problems. Guidance developed as a result of the consultations will be an important resource for ethics committees and CABS to draw upon.

International guidelines should offer general ethical advice in order to avoid bias against people who use drugs and unify criteria for ethical evaluation. Although consensus was reached regarding some controversial ethical problems, an overarching question throughout the consultation involved the status of the ethical recommendations made in the guidance document.

As was the case in other consultations, the following recommendations should be read keeping in mind that “ethical guidance is often vague and leaves leeway for discretion, judgment, and common sense, given the conditions and circumstances of a particular research project”.[51]

[51] Kuala Lumpur Consultation Meeting Report.

KEY RECOMMENDATIONS

1- Given the decrease in drug injecting in Latin America and the Caribbean and the high risk of HIV acquisition among people who use illicit drugs in general, it was recommended that the new guidance should apply to all people whose illicit drug use places them at higher risk of acquiring HIV. The title and text of the guideline should be modified accordingly.

2- Community participants may contribute to set future research agendas by suggesting objectives that are not among those originally set out as primary objectives in research protocols, but which are consistent with the community's concerns and needs.

3- A clear definition of a Community Advisory Board (CAB) or Mechanism (CAM) ought to be provided in the *Good participatory practice guidelines* in order to avoid problems confronted in the past in the creation and organization of CABs/CAMs.

4- Since local authorities may compromise participants' well-being and limit the feasibility of a study, the questions of which authorities to involve and the best ways of involving them should be addressed through a close examination of the local context. Two strategies were suggested: first, a bottom-up strategy designed to protect participants, and, second, a generalized strategy designed to make sure that no serious opposition will threaten the overall conduct of the study.

5- When close examination of the context reveals that local authorities could pose a potential risk to trial participant well-being, researchers may identify community facilitators to assist in gaining access to the community of people who use drugs.

6- Pregnant or breastfeeding women who use drugs should not be included in a trial unless there is a reason to believe that there is specified degree of safety with the biomedical HIV prevention approach in this population. Research should be in an advanced stage before pregnant or breastfeeding women are included in a trial.

7- In countries where abortion is criminalised or therapeutic abortion is not easily accessible, pregnancy in a trial participant is most likely to result in the birth of a person whose interests and well-being should be taken into account. In deciding whether to include pregnant women in a trial, researchers should take into account the best interests of the person that will be born as well as the interests of the women in question.

8- Before enrolling children and adolescents who use drugs in a study, the y should be asked whether their parents are aware of their drug use behaviour and whether they would allow for their parents to be asked to provide consent for their enrolment.

9- When possible, contact with children and adolescents should be made through drug treatment centres in order to minimize public exposure and stigma. If legislation does not require parental consent for involving minors who attend such centres in research, this should be the preferred option.

10- All research subjects should be evaluated and receive continued adequate care and treatment, including antiretroviral therapy when eligible, at the end of the trial if seroconversion occurred during trial participation. One option for assuring access to necessary post-trial treatment is to require sponsors to provide treatment for research participants unless the government provides it free of charge to the entire population.

11- The different types and sources of vulnerability of people who use drugs should be adequately acknowledged. During the consultation, the model of “layers of vulnerability” was recommended for distinguishing, analysing, and addressing the various needs of vulnerable populations. Special attention should be granted to those layers of vulnerability that might infringe on participants’ privacy.

12- CABs and ethics committees should be aware of the vulnerability layers of people who use drugs in order to adequately protect these populations. Local CABs and ethics committees should be consulted in order to evaluate the vulnerability layers of people who use drugs.

13- Researchers should be trained in bioethics and human rights.

14- During the process of informed consent, all risks related to legal and regulatory sanctions should be explicitly addressed, whether they are drug-related or not. Awareness of the risks of incarceration due to the criminalisation of drug use and drug trafficking must not be taken for granted and must be explicitly discussed with potential participants.

15- Researchers need to address all possible instances in which reporting of participants to local authorities may be necessary, whether these are moral or legal. If, for example, there is no legal requirement for reporting child abuse, a researcher should still inform potential participants if child abuse will be reported due to moral concerns. The issue of notifying sexual partners about the HIV status of a potential trial participant is context specific and it was recommended that this not be addressed explicitly in the new guidance point.

16- The possibility of involuntary and voluntary reclusion must be explicitly considered in the informed consent process, and people who use drugs should be asked whether the researchers can try to contact them should they miss study visits. If the participant agrees to be contacted in such instances, further information must be gathered about who can be contacted and the kind of information that can be obtained from third parties regarding the situation of participants.

17- Considering the high rate of psychiatric comorbidities that affect people who use drugs, the level of a potential participant's comprehension should be assessed in the most comprehensive way, in order to assure that a subject’s participation is truly voluntary. In the case of acute intoxication, the informed consent process must be interrupted and enrolment postponed until the acute effects of substances that might distort judgment and perception are over.

18- Respect for the autonomy of people who use drugs requires that no basic difference be made with respect to people participating in similar trials who do not use drugs. In order to avoid paternalistic and discriminatory attitudes towards people who use drugs, the amount of remuneration must be calculated in the same way as is done for other research participants with similar incomes who take on equivalent burdens and time commitments.

19- Whether there should be differences in the kind of remuneration to be given to different groups of drug users, is a question to be answered by CABs and ethics committees.

20- A general category entitled “Gender” should be added. It should be subdivided into several subcategories, such as MSM, transgender, and intersex to address the ways in which various gender identities can present different layers of vulnerability.

21- Although there was no consensus as to how race and ethnicity should appear in the guidelines, these categories and the associated vulnerability layers should be explicitly considered in the Ethical Considerations guidance document.

22- Since the humanitarian principles established in the Kuala Lumpur consultation for conducting research in compulsory drug detention centres can rarely be met –if at all- in closed settings, research should not be conducted in closed settings. This implies both that research should not start in these contexts and that participants should be discontinued from research when entering a reclusive environment.

23- To the extent that it is feasible, participants should retain the benefits of trial participation when entering a reclusive setting. However, this may require further consideration, since ethical and logistical difficulties may arise. The extent and weight of these concerns will vary according to each particular context, and researchers and sponsors should consider on a case-by-case basis whether it is feasible and ethically admissible that the benefits of the research be continued during detention.

24- Researchers should explicitly consider in the protocol under what circumstances participants can be re-incorporated into research upon their release from detention.

25- Change in drug use behaviour should not disqualify research participants from re-entering a trial post-release.

26- Participation in a trial and access to its benefits should not be compromised by changes in drug behaviour, especially if the participant ceases to use drugs or moderates drug consumption.

27- Researchers should make efforts to arrange a final meeting with incarcerated research participants when participants enter a reclusion setting, and prior to discontinuing them from research, in order to obtain relevant data.

28- In designing the research protocol, researchers must take into consideration the potential loss to follow up of participants due to reclusion and make the necessary arrangements so that the validity of the data is not jeopardized.

29- In order to attend to the special needs of people who use drugs, integrated care and treatment strategies should be promoted in the region. Suitably trained personnel should have experience in evidence-based approaches for treating drug use disorders and experience in psychiatric care and management of psychiatric patients. In the case of treating HIV-positive patients who use drugs, they should have experience in HIV treatment and be aware of how drug use, antiretroviral therapy, and drug treatment regimens might interact and affect one another. Research teams should also include people with training and experience in integrated care.

30- Protocols should define the procedures to be taken when research participants threaten members of the research team or other trial participants.

31- In order to benefit the research population and contribute to capacity building, researchers should present the relevant authorities with an analysis of how the research might inform the improvement of local health care and treatment practices and related public policies.

32- Researchers should make plans for referring trial participants to specialized care, including full access to psychosocial and psychiatric care, as well as attention to emergencies directly associated with the misuse of substances (e.g. overdose management). These measures should be defined before the study begins and be guaranteed over its course.

33- Intervention trials should provide full access to care for medical conditions that emerge during the study, whether directly or indirectly related to the trial. Researchers should appeal to the best available resources, methods, and professionals in each specific context.

34- Activities aimed at reducing drug-related harms, including provision of the standard package of prevention approaches, as defined by international agencies, may not always harmonize with local legislation. There was no consensus as to how researchers should proceed with respect to the moral imperative of providing proven state-of-the-art HIV prevention and harm reduction methods when these conflict with local regulations.