別紙様式第 2-1

別紙 3-1

医薬品
医薬部外品　研究報告　調査報告書
化粧品

識別番号・報告回数		回	報告日 年　月　日	第一報入手日 2006 年 9 月 29 日	新医薬品等の区分 該当なし	総合機構処理欄
一般的名称			研究報告の公表状況	Guideline on validation of immuno-assay for the detection of antibody to human immunodeficiency virus (anti-HIV) in plasma pools. European Medicines Agency (2006).	公表国 米国	
販売名（企業名）						

研究報告の概要	使用上の注意記載状況・その他参考事項等
調査書類の評価中に見受けられた，プール血漿の抗ヒト免疫不全ウイルス (抗 HIV) 検査におけるバリデーションの不備のある点を改善するためにこのガイドラインが作成された。抗 HIV イムノアッセイ法は血漿分画製剤の原料となるプール血漿の抗 HIV-1 および抗 HIV-2 抗体を検出する定性試験である。しかし，市販の抗 HIV 検出キットは個人供血サンプルに対してのみバリデーションされている。したがって，血漿分画製剤用プール血漿における検査・バリデーションが必要となる。しかし，プール血漿の血清学的検査は，ウイルス感染の安全性の保証を意味するのではなく，GMP ガイドラインに対する重大な不備を検出する方法とみなされるべきである。市販キットのバリデーションとは，頑健性 (信頼性) はもちろん，特異性と検出感度 (抗原の検出限界値やカットオフ値) の決定を含む多段階プロセスである。加えて，分析法内・分析法間での変動も多数の方法を用いて行うべきである。試験方法は，準備，保管管理，試験，再試験，及び判定の手順に関する情報を含む標準作業手順書 (SOPs) で文書化されなければならない。また，検査キットに非依存性の弱い陽性コントロール (個人供血のカットオフ値の 2-3 倍) を試験ごとに組み入れるべきである。陽性サンプルは，複数の異なる抗原を用いてバリデーションされたイムノアッセイで陰性と実証されない限りは，陽性と見なすべきである。核酸増幅検査 (NAT) は陰性を実証する方法としては使用不可能である。	BYL-2007-0242

報告企業の意見	今後の対応
EMEA から発行された本ガイダンスは，血漿分画製剤に使用されるプール血漿の HIV-1 および HIV-2 抗体スクリーニングの改善と標準化を目的としている。EMEA は，個人供血の試験用に開発された市販の抗 HIV 検出キットをプール血漿に適応する場合，バリデーションを完全に行うよう勧告している。バリデーションされた確認法は陽性サンプルの再試験に対しても実施すべきであると考える。また，医薬品市販承認取得者と血漿マスターファイル所持者はこのガイドラインに照らし合わせてプール血漿の試験法のバリデーションを検討する必要がある。	本ガイドラインに記載された重要事項に対して，弊社の血漿分画製剤に使用されるプール血漿は，既存のバリデーションで適用できていることが確認されていることから，現時点では新たな対応は必要ない。

(13)

European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

London, 21 September 2006
EMEA/CHMP/BWP/298388/05

COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP)

GUIDELINE ON VALIDATION OF IMMUNOASSAY FOR THE DETECTION OF ANTIBODY TO HUMAN IMMUNODEFICIENCY VIRUS (ANTI-HIV) IN PLASMA POOLS

DRAFT AGREED BY BIOLOGICS WORKING PARTY	June 2005
ADOPTION BY CHMP FOR RELEASE FOR CONSULTATION	June 2005
END OF CONSULTATION (DEADLINE FOR COMMENTS)	31 December 2005
AGREED BY BIOLOGICS WORKING PARTY	September 2006
ADOPTION BY CHMP	September 2006
DATE FOR COMING INTO EFFECT	1 April 2007

KEYWORDS	Anti-HIV

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GUIDELINE ON VALIDATION OF IMMUNOASSAY FOR THE DETECTION OF ANTIBODY TO HUMAN IMMUNODEFICIENCY VIRUS (ANTI-HIV) IN PLASMA POOLS

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VALIDATION OF IMMUNOASSAY FOR THE DETECTION OF ANTIBODY TO HUMAN IMMUNODEFICIENCY VIRUS (ANTI-HIV) IN PLASMA POOLS

Introduction

Immunoassays for the detection of antibodies to Human Immunodeficiency Virus (anti-HIV) are qualitative tests for the presence of anti-HIV in pooled plasma for fractionation. The validation requirements are laid down in the following documents:

- The test is considered to be a qualitative limit test for the control of impurities. Therefore, according to the "Note for guidance on validation of analytical procedures: definitions and terminology (CPMP/ICH/381/95)", ICH topic Q2A, the two characteristics regarded as the most important for validation of the analytical procedure are specificity and the detection limit. However, the note for guidance adds "those validation characteristics are regarded as the most important, (...) but occasional exceptions should be dealt with on a case-by-case basis" and Q2A requires that robustness needs to be considered.
- The Ph. Eur. Monograph 01/2005:0853 "Human plasma for fractionation" requires the use of anti-HIV test methods of suitable sensitivity and specificity for plasma pool testing.
- The "Note for guidance on plasma derived medicinal products" (CPMP/BWP/269/95, 3.2.2) specifies that the sensitivity of the test in relation to pool size has to be stated. The intention of the test is defined to be a safeguard against errors in testing or pooling.
- The Ph. Eur. chapter 2.7.1 "Immunochemical methods" requires the use of international reference material. Furthermore, the chapter suggests the use of commercial assay kits.
- The GMP Guide (Volume 4, Chapter 6, 6.21) as well as ISO 17025 (4.6.2) require critical reagents to be under control.

In accordance with these guidelines, the validation characteristics are described as:

- Specificity is the ability to unequivocally assess antibodies to HIV in the presence of other components, which may be expected to be present.
- The detection limit of an individual analytical procedure is the lowest amount of analyte in a sample, which can be detected but not necessarily quantitated as an exact value. In the context of plasma pool testing for anti-HIV, the detection limit should be expressed as endpoint dilution titre(s) of well-characterised positive samples.
- The robustness of an analytical procedure is a measure of its capacity to remain unaffected by small but deliberate variations in method parameters and provides an indication of its reliability during normal performance.

Validation Guidelines

1. SCOPE

Anti-HIV assay kits, for single donation purposes, marketed in Europe are CE-marked devices and are classified in Annex II A of the Directive 98/79/EC on in vitro diagnostic medical devices. The kits are therefore subject to the Common Technical Specifications (CTS, 2002/364/EC)

Anti-HIV assay kits are validated for use in single donation testing either through CE-marking in the EU or through non-EU regulation. The use of such assays for the testing of pooled plasma for fractionation is a change of the intended use and this application is not covered by the validation undertaken by the test kit manufacturer. The application for testing plasma pools for fractionation therefore has to be accompanied by appropriate validation.

If non-CE marked test kits are used for plasma pool testing purposes, equivalent quality to a CE-marked test kit for individual donation testing should be proven in addition to the validation for pool testing described in this guideline.

The CTS defines minimal requirements for diagnostic sensitivity for assay kits.

Furthermore, the CTS requires that specificity should be demonstrated in a broad variety of patient samples. However, this approach to validation is not necessarily relevant for plasma pool testing purposes, because those patient samples which may give aberrant responses (e.g., those from patients with autoimmune diseases or having cross-reactive infections) will normally have been excluded by the donor selection process. In addition, non-specific interfering factors will be diluted in the plasma pool.

Plasma pool serology is not capable of detecting all contaminated single donations that may have escaped single donation screening. Anti-HIV is not a defined analyte, but can be described as the sum of reactivity of an individual humoral immune response to a virus subject to high genetic variability. In particular, samples from early infection stages contain low affinity antibodies that show poor dilution kinetics.

Plasma pool serology should therefore not be considered as a test to ensure viral safety, but as a measure to detect serious GMP failures.

This document describes methods to select and validate commercial qualitative immunoassay test kits for assessing contamination of plasma pools with antibodies to HIV 1 and 2 based on the above mentioned documents.

2. SELECTION OF THE TEST KIT(S)

Commercial kits used for the analytical procedure are validated by the manufacturer for single donation testing only. Selection of a test kit for plasma pool testing should be based on high dilutional sensitivity. As preliminary selection criterion, relative end point dilution titres of a well-characterised positive sample (e.g. a commercial working Standard) should be compared.

In most cases, the manufacturer's instructions for use of reagents are adequate for the performance of the test procedure on plasma pools.

Any modification of the manufacturer's instructions should be included in the validation of use of a kit for testing plasma pools.

Evaluation criteria of the manufacturer may be adapted to plasma pool testing according to validation data relevant to plasma pools (see 3.1 Specificity and determination of a cut-off limit for pool samples, and 4. Quality assurance).

3. VALIDATION

3.1 Specificity and determination of a cut-off limit for pool samples

For commercial kits the cut-off value established by the manufacturer is a compromise between sensitivity and specificity based on results from single donation testing. Many test kit manufacturers also define a 'grey-zone' cut-off which will identify samples which give a response above background but below the cut-off. It is recommended that such samples are re-tested as if they were reactive.

On the basis of previous experience in testing plasma pools, the use of a lower cut-off for pool samples should be considered as non-specific factors present in single donations are diluted in a fractionation pool. The use of such a cut-off will increase the analytical sensitivity of assays and facilitate the detection of a single positive donation in a plasma pool. The grey-zone value recommended by the kit manufacturer may be suitable. Alternatively, a limit could be established by considering the signal distribution of negative pools, e.g. as mean response to cut-off ratios of negative pool samples + 3 standard deviations and routinely expressed as % of single donation cut-off. In no case should the pool cut-off be higher than the single donation cut-off.

For all practical applications in the context of this Guideline, if a grey-zone limit is used as the cut-off value for pool samples, this limit is used to identify initially and repeatedly reactive plasma pools (see 5., confirmation strategies).

3.2 Robustness

Robustness of the analytical procedure has to be evaluated, as all methods using biological and biochemical reagents may be subject of considerable batch-to-batch variation of the reagents used and may be influenced by changes in ambient conditions.

3.2.1 Inter-assay and intra-assay

Qualitative immunoassays primarily produce a quantitative signal that is compared to the calculated cut-off in an independent step. Reactive plasma pool samples are likely to give low signals due to high dilution in the pool. Batch-to-batch variability of the test kit reagents (including controls) may have a significant influence on results and should be under control, as is foreseen by the GMP guide (chapter 6, 6.21) and ISO 17025 (4.6.2).

Robustness of the method should be demonstrated for a panel of representative negative pool samples (e.g. routine pool samples which have tested negative by both the manufacturer and an OMCL), and a low positive sample (e.g. the low positive control, see 4.3).

The study should cover:

- Inter-assay variability in 6 independent assays (including variable ambient conditions, equipment if available, preferably using more than one test kit lot if available)
- Intra-assay variability with at least 6 determinations of a low positive control in 1 run

  Intra-assay variability can be expressed as %CV (Relative Standard Deviation, RSD) of the signal of the low positive sample in relation to the cut-off of the individual assay (S/CO, sample to cut-off ratio).

3.3 Detection limit

There is no International Standard for antibodies to HIV 1 or 2. As anti-HIV is not a defined analyte, the detection limit (dilutional sensitivity) has to be determined with a representative panel of positive samples reflecting different subtypes and groups taking into consideration the epidemiological situation in the respective regions where the plasma is sourced. Confirmed reactive samples from routine donor screening may be regarded as representative without further characterization, so long as the number of samples in the panel covers the main genotypes.

To facilitate comparability of detection limit data, independent reference material for HIV-1 antibodies should be included in the panel as soon as it becomes available.

The panel is serially diluted in anti-HIV negative pool plasma. The minimum and maximum number of donations in a typical pool should be taken into consideration in the dilution series used to simulate the "best" and "worst"case scenarios. Results are expressed as end point dilution titres.

4. QUALITY ASSURANCE

4.1 Standard Operating Procedures for plasma pool testing

The test procedures must be described in detail in the form of standard operating procedures (SOPs). These should cover at least the following operations:

- Storage conditions for samples
- Preparation of samples (e.g. freezing/thawing steps, mixing)
- Description of the equipment and the test kit used
- Incubation procedures (including tolerance limits for time and temperature, e.g. according to the test kit manufacturer's specifications/instrument settings)
- Detailed formulae for calculation and interpretation of results
- Validity criteria for the individual assay

- Retesting procedures
- Reference to confirmation procedures, if applicable

4.2 Test kit controls

The test kit manufacturer's controls should always be included in every assay to ensure correct performance of reagents according to the manufacturer's specifications. Validity criteria for modified testing conditions should be defined and documented.

4.3 Test kit independent controls

The positive controls in many commercial test kits are highly reactive and therefore do not reflect the low level of reactivity likely to be found in contaminated pool samples. In addition, as for all biological reagents, these controls are subject of batch-to-batch variation. Therefore it is strongly advised to include an independent low positive control (in the dynamic range of the assay, e.g. 2-3 times the single donation cut-off) in every test used for on-going data monitoring.

4.4 Proficiency testing

Regular participation in an appropriate proficiency testing scheme which include diluted samples with low reactivity to assess the analytical sensitivity of kits is encouraged.

5. CONFIRMATION STRATEGIES

A validated confirmation strategy for initially reactive results should be in place. A pool is considered negative if the initially reactive sample gives a negative result when retested in duplicate. Repeat reactive samples have to be considered positive unless proven otherwise with an adequately validated serological method using different antigens.

A repeat reactive on repeat testing should be confirmed through the use of alternative assays. If immunoblots are used as HIV confirmation tests, great care in the formulation of interpretation criteria is advised, as the highly specific ENV bands are hardly detectable in high dilutions, and some pool samples show unspecific bands at 24 and 40 kDa. Therefore, a positive immunoblot may be used to confirm an initially reactive result. However, a negative immunoblot result should be treated with caution.

As anti-HIV may be present in donors with low or undetectable nucleic acid plasma levels, NAT should not be considered as a confirmation assay as a negative NAT results does not invalidate a positive serological result. On the other hand, positive NAT results do confirm the serological detection of contaminations.

6. IMPLEMENTATION OF THIS GUIDELINE

This guideline has been developed to respond to inadequacies in the validation of plasma pool testing for anti-HIV observed during evaluation of dossiers. Marketing Authorisation Holders and Plasma Master File Holders should review the validation of their pool testing methods in the light of this guidance. If the key aspects described in the guideline have already been covered by existing validation, no further validation is needed. If this is not the case, pool testing should be validated in accordance with this guideline and reported in the next annual update of the documentation on the plasma starting material.

医薬品 研究報告 調査報告書

識別番号・報告回数			報告日	第一報入手日	新医薬品等の区分	機構処理欄
				2007. 3. 19	該当なし	

一般的名称	解凍人赤血球濃厚液	研究報告の公表状況		公表国
販売名(企業名)	解凍赤血球濃厚液「日赤」(日本赤十字社) 照射解凍赤血球濃厚液「日赤」(日本赤十字社) 解凍赤血球-LR「日赤」(日本赤十字社) 照射解凍赤血球-LR「日赤」(日本赤十字社)		Hesketh T. Lancet. 2007 Feb 24;369(9562):621-3.	英国

研究報告の概要

○中国のHIV/AIDS:数の問題

HIV/AIDSの脅威に対する対応に失敗し、HIV/AIDSの規模を組織的に情報隠蔽した中国は大きな批判にさらされてきた。中国はハイリスク行為に対して法律の施行を中心とした試みに早期に着手したが、後に他国の効果的な施策から得られた教訓によって、エビデンスに基づいた施策を採用したことが報告された。最近発表されたAIDSの予防管理の規制は、中国全土での実施に大きなばらつきがあるとしても、エビデンスに基づく政策の良例である。

HIV感染者の割合は人口の0.05%(65万人)であり他の健康問題が多数あるにも関わらず、注目を集めた理由の一つは、複数の外部団体が行った感染規模の予測が過大な数値だったためである。2002年の国連の委託報告や米国国家情報会議(NIC)は、中国のHIV感染者は約100～200万人で感染爆発の危機が迫っていると推測した。他の研究所からも悲観的な予測値が示された。このような非常に不正確な予測から、様々な問題が生じる。まず、予測されたハイリスク群から一般集団への大規模なウイルスの拡散は起きておらず、根拠のない想定に基づいていたと言える。2番目に、複数の不正確な予測は、専門家でも扇情的な数値を算出の根拠に関係なく受け入れたことを示している。3番目として、過大で不正確な予測が及ぼした影響について問うべきである。中国では、こうした予測に基づいて国内、諸外国、多くの国際民間団体からの多額の援助資金を集めた。この資金は、HIV/AIDSの感染拡大を遅らせたかもしれないが、より必要性の高い領域に援助が届くことを妨げている。

中国でのHIV/AIDS対策はハイリスク地域を中心に行うべきである。

使用上の注意記載状況・その他参考事項等

解凍赤血球濃厚液「日赤」
照射解凍赤血球濃厚液「日赤」
解凍赤血球-LR「日赤」
照射解凍赤血球-LR「日赤」

血液を介するウイルス、
細菌、原虫等の感染
vCJD等の伝播のリスク

報告企業の意見	今後の対応
中国のHIV感染者は約100～200万人で感染爆発の危機が迫っていると推測されていたが、実際の感染率は人口の0.05%(65万人)であった。感染規模に関する誤った予測数は中国国内に様々な問題をもたらしたとの報告である。	日本赤十字社では、HIVについて20プールNATを含むスクリーニングを行い、陽性血液を排除している。国内外のHIV感染、AIDS発生の動向やHIV感染に関する新たな知見等について今後も情報の収集に努める。次世代NAT試薬についての評価、検査方法の改良に向けた開発・検討を進める。

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Moreover, today's technology drive may soon improve drug-eluting stents and their antithrombotic properties (eg, with use of resorbable drugs, polymers, and perhaps resorbable stents), removing the need for cumbersome long-term antiplatelet therapy and preventing the rare but devastating occurrence of late stent thrombosis.

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PU is a consultant for Cordis and Medtronic, and has received speakers' fees from Cordis, Medtronic, Boston Scientific, Terumo, and Datascope. EDB declares that he has no conflict of interest.

1 Serruys PW, Strauss BH, Beatt KJ, et al. Angiographic follow-up after placement of a self-expanding coronary-artery stent. *N Engl J Med* 1991; 324: 13–17.
2 Daemen J, Wenaweser P, Tsuchida K, et al. Early and late coronary stent thrombosis of sirolimus-eluting and paclitaxel-eluting stents in routine clinical practice: data from a large two-institutional cohort study. *Lancet* 2007; 369: 667–78.
3 Moreno R, Fernandez C, Hernandez R, et al. Drug-eluting stent thrombosis: results from a pooled analysis including 10 randomized studies. *J Am Coll Cardiol* 2005; 45: 954–59.
4 Weisz G, Moses J, Schofer J, et al. Late stent thrombosis in sirolimus-eluting versus bare metal stents in 4 randomized trials with 3-year follow-up. *J Am Coll Cardiol* 2006; 47 (suppl 2): 8B (abstr 2801-3).
5 Pfisterer M, Brunner-La Rocca HP, Buser PT, et al. Late clinical events after clopidogrel discontinuation may limit the benefit of drug-eluting stents. *J Am Coll Cardiol* 2006; 48: 2584–91.
6 Kastrati A, Dibra A, Eberle S, et al. Sirolimus-eluting stents vs paclitaxel-eluting stents in patients with coronary artery disease. *JAMA* 2005; 294: 819–25.
7 Spaulding C, Henry P, Teiger E, et al. Sirolimus-eluting versus uncoated stents in acute myocardial infarction. *N Engl J Med* 2006; 355: 1093–104.
8 Moses JW, Leon MB, Popma JJ, et al. Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. *N Engl J Med* 2003; 349: 1315–23.
9 Stone GW, Ellis SG, Cox DA, et al. A polymer-based paclitaxel-eluting stent in patients with coronary artery disease. *N Engl J Med* 2004; 350: 221–31.
10 Urban P, Gershlick AH, Guagliumi G, et al. Safety of coronary sirolimus-eluting stents in daily clinical practice: one year follow-up of the e-Cypher registry. *Circulation* 2006; 113: 1108–13.
11 Cutlip DE, Chhabra AG, Baim DS, et al. Beyond restenosis—five-year clinical outcomes from second-generation coronary stent trials. *Circulation* 2004; 110: 1226–30.
12 Chen MS, John JM, Chew DP, et al. Bare metal stent restenosis is not a benign clinical entity. *Am Heart J* 2006; 151: 1260–64.
13 Motwani J, Topol EJ. Aortocoronary saphenous vein graft disease pathogenesis, predisposition and prevention. *Circulation* 1998; 97: 916–31.
14 Wenaweser P, Rey C, Eberli FR, et al. Stent thrombosis following bare-metal stent implantation: success of emergency percutaneous coronary intervention and predictors of adverse outcome. *Eur Heart J* 2005; 26: 1180–87.

HIV/AIDS in China: the numbers problem

China has been widely criticised for its failure to respond to the HIV/AIDS threat and for systematic suppression of information about the size of the problem.[1,2] Thus Zunyou Wu and colleagues' report in today's *Lancet* of the way in which China has responded to HIV/AIDS will surprise many.[3] Their thorough review shows how much progress has been made, and how, given the political and cultural context, the Chinese response has evolved in a measured and mainly appropriate way.

Wu and colleagues show how early efforts emphasised enforcement of laws against high-risk behaviour, but that later lessons from effective interventions in other countries (eg, needle-exchange programmes in Australia and condom campaigns for sex workers in Thailand) have led to a more evidence-based approach. The process of policy development might not have been as neat as that presented because of tensions, particularly those between public-health officials and the police and those within public security over the management of illegal drug use and prostitution. However, the recently announced AIDS Prevention and Control Regulations[4] are a good example of evidence-based policy, even if their implementation is highly variable across China.

The most surprising feature of HIV/AIDS in China is how it has attracted such attention and large amounts of external funding, given that the proportion of the

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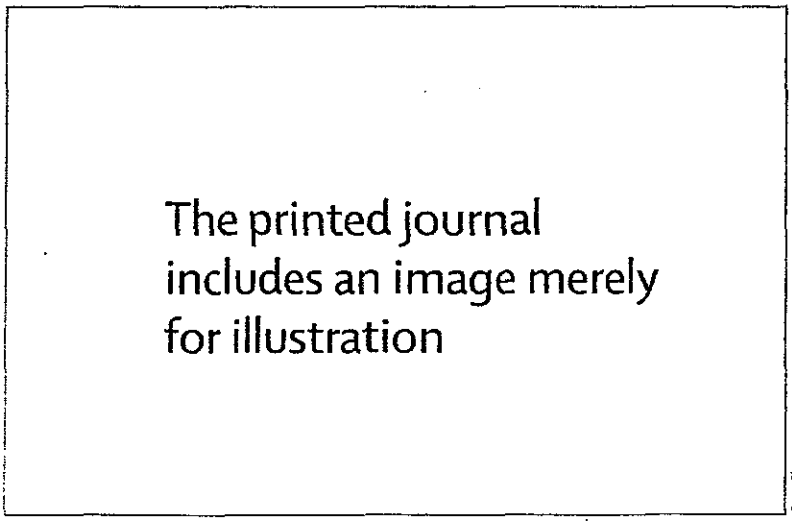

Famous Pictures

Patient with AIDS in China

population with HIV/AIDS is only 0·05% and that there are many other more pressing health issues in China. Part of the reason for this attention is because predictions of the size of the epidemic were substantially overestimated by several expert bodies. In 2002, a UN-commissioned report, emotively entitled *China's Titanic peril*,[5] estimated that China had about 1 million cases of HIV, and that it was on the brink of an "explosive HIV/AIDS epidemic...with an imminent risk to widespread dissemination to the general population". The report continued: "a potential HIV/AIDS disaster of unimaginable proportion now lies in wait." A few months later, the US National Intelligence Council estimated that 1–2 million people were living with HIV in China, and predicted 10–15 million cases by 2010.[6] The National Intelligence Council claimed that these figures were more reliable than previous estimates because they did not rely on official sources, which the National Intelligence Council asserted "systematically understate the actual figures", but rather incorporated assessments by academics and non-governmental organisations working in the field.

Other reports at this time were similarly emotive and pessimistic: from the Centre for Strategic and International Studies (Washington, DC, USA), HIV/AIDS was referred to as China's timebomb;[7] and from the American Enterprise Institute as the AIDS typhoon.[8] The latter report emphasised the probable damage to the economy because HIV would spread among young educated urban people. That China had a massive potential HIV problem became received wisdom. However, as Wu and colleagues note, by 2006 the number of people living with HIV/AIDS is estimated to be 650 000—a figure revised downwards by 200 000 from 2005.[9]

Such wildly inaccurate predictions raise several issues. First, how was the figure of 10–15 million cases by 2010 calculated? This estimate assumes substantial spread of the virus from high-risk groups to the general population, yet the few population studies and, in particular, trends from sentinel surveillance of pregnant women in high-risk areas show that such spread has not occurred.[10–12] Therefore, these predictions were made on unfounded assumptions. Second, the inaccurate predictions show how even well-respected groups willingly accept and repeat a number (especially one that is high and sensationalist) irrespective of the assumptions of the underlying calculations, starting a cycle: repeat something often enough and everyone believes it. Third, we should ask what the effects of these high and inaccurate predictions have been. In China, they certainly galvanised activity, attracting large funds from domestic sources (beautifully illustrated by figure 5 in Wu and colleagues' review), international sources (including bilateral donors, notably the UK's Department for International Development and the Australian Government's overseas aid programme, AusAID), and many international non-governmental organisations.

Such funding might have helped slow the spread of the epidemic. However, a disproportionate amount of funding is being given to a health problem for which the disease burden is low, drawing resources away from areas of greater need. For example, China's burden of disease from tobacco use is enormous.[13] If similar resources were devoted to tobacco-control measures, the effect could be huge. The added irony: in a fee-for-service system, individuals can receive free HIV treatment in many areas of China, whereas others have to pay for tuberculosis treatment, drugs for hypertension, or for cataract surgery.

Wu and colleagues call for a scaling-up of HIV/AIDS activities in China. This effort should focus on high-risk areas. For most of China, the prevalence of HIV remains low. Here, the focus of public-health efforts should be on diseases with a higher burden.

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I declare that I have no conflict of interest.

1 Asia Division, Human Rights Watch. Locked doors: the human rights of people living with HIV/AIDS in China. *Human Rights Watch* 2003; 15: 1–95.
2 Ruger JP. Democracy and health. *QJ Med* 2005; 98: 299–304.
3 Wu ZY, Sullivan S, Wang Y, Rotheram MJ, Detels R. Evolution of China's response to HIV/AIDS. *Lancet* 2007; 369: 679–90.
4 China AIDS Info. http://www.china-aids.org/english/aidsreg-2006-intro (accessed Oct 26, 2006).
5 Eldis gateway. HIV/AIDS: China's Titanic peril: 2001 update of the AIDS situation and needs assessment report. UNAIDS, 2002. http://www.eldis.org/static/DOC9892.htm (accessed Oct 26, 2006).
6 National Intelligence Council. The next wave of HIV/AIDS: Nigeria, Ethiopia, Russia, India, China. ICA 2002-04 D. September, 2002: http://www.fas.org/irp/nic/hiv-aids.html (accessed Oct 26, 2006).
7 Bates G, Morrison SJ, Thompson D, eds. Defusing China's timebomb—sustaining the momentum of China's HIV/AIDS response. A report of the CSIS HIV/AIDS delegation to China, April 13–18, 2004. 2004: http://www.csis.org/media/csis/pubs/040413_china_aids.pdf (accessed Oct 26, 2006).

8 American Enterprise Institute, Washington, D.C. Can Asia avoid the AIDS typhoon? Nov 11, 2002: http://www.kaisernetwork.org/health_cast/hcast_index.cfm?display=detail&hc=721 (accessed Oct 19, 2006).

9 Ministry of Health, People's Republic of China, Joint United Nations Programme on HIV/AIDS, World Health Organization. Update on the HIV/AIDS epidemic and response in China. 2006: http://data.unaids.org/publications/External-Documents/RP_2005ChinaEstimation_25Jan06_en.pdf (accessed Oct 26, 2006).

10 Hesketh T, Huang XM, Wang ZB, Xing ZW, Cubitt DW, Tomkins AM. Using the premarital examination for population-based surveillance for HIV in China. *AIDS* 2003; 17: 1574–76.

11 Qu S, Sun X, Zheng X, Shen J. National sentinel surveillance of HIV infection in China from 1995 to 2001. XIV International AIDS Conference, Barcelona, Spain, July 7–12, 2002: WePeC6072 (abstr). http://gateway.nlm.nih.gov/MeetingAbstracts/102250025.html (accessed Oct 26, 2006).

12 Hong L, Mo LH, Liu H. Prevention of HIV transmission from mother-to-child in Yunnan. *Mod Prev Med* 2001; 28: 68–69.

13 Wang L, Kong L, Wu F, Bai Y, Burton R. Preventing chronic diseases in China. *Lancet* 2005; 366: 1821–24.

HIV-1 in Taiwan

Taiwan is entering a new and dangerous phase of its HIV-1/AIDS epidemic. By the end of 2006, 13702 individuals (including 599 foreigners) had been reported as infected with HIV-1 to the Centers for Disease Control of Taiwan.[1] In 2003, HIV-1 rates in first-time blood donors, military conscripts, and pregnant women were measured at 5·2, 57·0, and 12·0 per 100000, respectively.[2] Data from that year indicated HIV-1 rates of 0·09% for intravenous drug users, 0·2% for female sex workers, 1·9% for patients with sexually transmitted infections, and 6·7% for men who have sex with men in saunas or bath houses.[3] Since then, the number of people living with HIV-1/AIDS in Taiwan has jumped sharply, from an 11% increase in 2003 to a 77% increase in 2004 and a 123% increase in 2005 (figure 1).[1]

However, after the implementation of a harm-reduction programme, a 10% decrease was seen in 2006 (figure 1). The current estimated number of HIV-1/AIDS cases in Taiwan is about 30000, which suggests that the infection rate there could be greater than that in China: 30000 per 23 million (1/767) compared with 650000 per 1·3 billion (1/2000).[2]

A risk-factor analysis of reported cases showed that the proportion of intravenous drug users infected with HIV-1 increased from 1·7% (13/772) in 2002, to 8·1% (70/862) in 2003, to 41·3% (628/1520) in 2004, to 72·4% (2461/3399) in 2005, and dropped to 68·6% (2017/2974) in 2006 (figure 2).[1] The most important risk factor for Taiwanese intravenous drug users is needle-sharing, followed by the sharing of heroin diluents.[3] A molecular epidemiological study showed that more than 95% of intravenous drug users with newly diagnosed HIV-1 in 2004 and 2005 were infected with CRF07_BC, a circulating recombinant form of subtypes B′ and C.[4,5] Previously, several studies suggested that CRF07_BC originated in China's Yunnan province as a mix of subtype B′ from Thailand and subtype C from India. The subtype is believed to have moved to Xinjiang province in China's northwest along a major heroin-trafficking route.[6]

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Of the 60000–100000 intravenous drug users in Taiwan, 10–15% may be infected with CRF07_BC. If so, they probably represent the largest group of such intravenous drug users in northeast Asia. The circulating recombinant form might have followed a separate drug-trafficking route to Taiwan from Yunnan

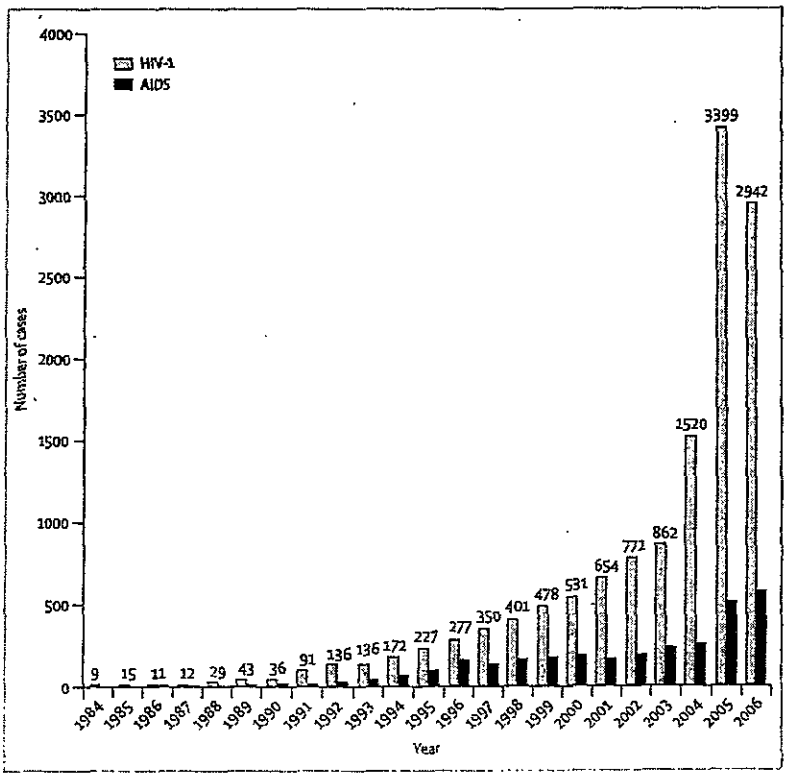

Figure 1: Annual numbers of HIV-1 seropositive cases and AIDS patients reported to Taiwan Centers for Disease Control[1]