NEWS

DRUG COMPANIES AGREE TO MAKE CLINICAL TRIAL RESULTS PUBLIC

Pharmaceutical companies around the world recently agreed to make results from clinical trials of new prescription medicines publicly available.

The voluntary agreement has been drawn up by the world's main pharmaceutical industry trade associations and agreed by key companies. It states that summary results of completed, industry sponsored clinical trials will be publicly disclosed on free and publicly accessible databases, regardless of outcome, for any medicine approved for marketing in at least one country. The results will be published in a standard, non-promotional summary that will include a description of trial design and methods, results of primary and secondary outcome measures described in the protocol, and safety results.

Each company can select the website where they publish trial results, but if published in a peer-reviewed journal, the database will include a link to the relevant article.

For medicines not yet approved or for trials not yet completed, companies agreed that the results should normally be published within 1 year of approval or, for post-approval trials, within 1 year of trial completion. In addition, details of all clinical trials, other than exploratory trials, will be publicly registered within 21 days of starting patient enrolment, with information on how to enrol for patients and clinicians.

The agreement says that the pharmaceutical industry is 'committed to increasing the transparency of the clinical trials our member companies sponsor'. Four key international pharmaceutical associations, including the European Federation of Pharmaceutical Industries and Associations, and the Pharmaceutical Research and Manufacturers of America, signed the agreement, which will be adopted later this year. The agreement follows several serious problems with prescription medicines associated with lack of open access to clinical trial results, including the increased risk of cardiovascular deaths resulting in the recent withdrawal of rofecoxib. The principal policy adviser in health to Which?, a UK consumer organisation and publisher of *Drug and Therapeutics Bulletin*, said 'We support the agreement but consider that it should be mandatory – enforced by legislation – and not voluntary.'

Source: **www.bmj.com** (*BMJ* 2004; **329:** 816).

700 000 PEOPLE LIVING WITH AIDS IN DEVELOPING COUNTRIES NOW RECEIVING TREATMENT

By the end of 2004, 700 000 people living with AIDS in developing countries were receiving antiretroviral treatment (ART) thanks to the efforts of national governments, donors and other partners. This is an increase of approximately 75% in the total number receiving treatment from a year ago, and is up from 440 000 in July 2004.

At a joint press conference at the World Economic Forum's Annual Meeting, Switzerland, the World Health Organization (WHO), the Joint United Nations Programme on HIV/AIDS (UNAIDS), the United States Government and the Global Fund to Fight AIDS, Tuberculosis and Malaria revealed the results of their joint efforts to increase the availability of ART in poor countries.

However, all the organisations warned that major, continued efforts are needed in countries and internationally to continue working towards the goal of access to treatment for all who need it.

Treatment is happening because national governments are taking the lead to co-ordinate efforts with all partners to scale up treatment in rural and urban areas. The Global Fund is providing flexible funds to governments and projects. The USA is funding and providing technical assistance and guidance for programme and capacity development to support national strategies. The WHO and UNAIDS are providing guidance and technical assistance to help countries turn finance into programmes. NGOs, faith-based organisations, networks of people living with HIV/AIDS and the private sector are all contributing.

In the region with the heaviest burden – sub-Saharan Africa – the number of people on treatment has doubled over 6 months from 150 000 to 310 000. In Asia, the figure has doubled since June 2004 from 50 000 to 100 000.

The WHO and UNAIDS estimate that at the end of 2004 around 6 million people were in need of treatment in developing countries. In December 2003 WHO, UNAIDS and UN partners announced the '3 by 5' target, challenging countries to get 3 million people or half of those in need on treatment by the end of 2005.

FINAL RESULTS FROM FIELD EFFICACY TRIAL OF INTRANASAL FLU VACCINE

ID Biomedical Corporation recently announced that it has completed analysis of the vaccine immunogenicity and safety data from its 2003/2004 field efficacy trial of a non-living, intranasally delivered influenza vaccine.

As previously reported, both one- and two-dose regimens were efficacious in preventing influenza-like illness in association with a positive influenza virus culture and no vaccine recipient experienced febrile illness associated with culture-confirmed influenza.

With regard to safety, there was no statistically significant association of local or respiratory complaints (runny nose,

stuffy nose, itchy nose, nose bleed, sneezing, sore throat, red or puffy eyes, wheezing or cough) with active vaccine when compared with placebo (saline). Similarly, neither temperature elevations nor systemic complaints (headache, muscle or joint aches, tiredness, or loss of appetite) were related to receipt of the vaccine at either dosage level.

Throughout the study period, there was no statistically significant difference in the overall incidence of adverse events reported between the vaccine and placebo groups.

Source: **http://www.idbiomed.com/**

INSIGHT INTO THE ORIGINS OF THE AIDS EPIDEMIC MAY OFFER NEW TREATMENT APPROACHES

UK Medical Research Council (MRC) scientists have uncovered an important clue to understanding the origins of the AIDS epidemic. The work suggests that harnessing natural mechanisms of resistance to HIV infection might provide new methods for combating AIDS. The research team at the MRC's National Institute for Medical Research pinpointed crucial differences in a gene found in rhesus monkeys that can prevent HIV infection, and its human counterpart, that cannot.

The differences indicate that HIV infection would not have become established in the human population if the form of the gene present in certain monkeys had also been present in humans. More importantly, the studies reveal that only a single change to the human gene is needed to enable it to interfere with the replication process of the HIV virus and prevent infection.

Lead scientist, Dr Jonathan Stoye, said 'In theory, it should be possible to take cells from an HIV-infected individual, make them resistant to HIV infection with the modified gene and reintroduce them into the patient. These cells could then block progression to AIDS. Alternatively we could search for drugs that activate the human gene against HIV.'

Source: **http://www.mrc.ac.uk/**

CALCIUM BOOST TO YOUTHS' BONES COULD REDUCE OSTEOPOROSIS RISK

New research on calcium and bone development suggests that efforts to prevent osteoporosis, generally considered a geriatric disease among women, could actually start before puberty.

In the study at the Ohio State University (OSU) Medical Center, which is the first clinical trial to track calcium's effects on bone density in girls aged 8 - 13 for as long as 7 years, researchers found that calcium supplementation significantly increased bone mass development during a critical childhood growth spurt. The findings suggest that elevated calcium use by pre-adolescent girls is likely to help prevent fractures and osteoporosis much later in life, said Velimir Matkovic, lead author of the study and director of the Osteoporosis Prevention and Treatment Center and the Bone and Mineral Metabolism Laboratory at OSU Medical Center.

The research is published in the January 2005 issue of *The American Journal of Clinical Nutrition* and *The Journal of Nutrition*. 'The importance of preventing osteoporosis can't be overstated,' Matkovic said. 'Prevention of this disease will not only improve the population's quality of life, but will also undoubtedly save on the skyrocketing health care costs associated with treatment.'

An estimated 30 million American women either have or are at risk of osteoporosis. Although the risk of losing bone mass is part of ageing, having the strongest skeleton possible as a youngster can tip the balance toward better bone health in later years, Matkovic said. The study also suggested that in addition to long-term benefits to women, high calcium intake during childhood shows signs of preventing bone fragility fractures in girls.

The 7-year length of the study allowed researchers to determine that calcium supplementation has the most significant effect on girls' bone build-up during the teenage growth spurt, and that over time, after the onset of menstruation, calcium supplementation's effects on bone density decreased. The calcium-supplemented group among the 354 girls in the trial showed a faster rate of bone mass development from the beginning of the study. The biggest difference in bone mineral density between the supplemented and non-supplemented groups of girls occurred from between 1 year before and 1 year after the onset of menstruation. By young adulthood, significant effects remained at the metacarpals in the hands, the forearm and the hip.

The researchers noted that the calcium requirement for growth is body-size specific; taller individuals need more calcium during growth than shorter individuals.

Source: **http://www.osu.edu**

REVIPARIN EFFECTIVE IN REDUCING RISK OF DEATH AFTER HEART ATTACK

The drug reviparin (a low molecular weight heparin anticoagulant), when administered to patients with a heart attack, is effective in reducing the risk of death and subsequent heart attack, according to a study in *JAMA*.

Approximately 15.5 million cardiovascular deaths occur in the USA every year. Although reperfusion therapy, aspirin, beta-blockers, and angiotensin-converting enzyme (ACE) inhibitors reduce the risk of death when used early after a heart attack, the rate of death and illness remains high. No

antithrombotic or newer antiplatelet drug has been shown to reduce the risk of death after a heart attack.

Salim Yusuf, DPhil, FRCPC, of Hamilton General Hospital and McMaster University, Ontario, Hamilton, Canada, and colleagues evaluated the effects of reviparin on the composite outcome of death, heart attack and stroke at 7 and 30 days. The randomised, double-blind, placebo-controlled trial (Clinical Trial of Reviparin and Metabolic Modulation in Acute Myocardial Infarction Treatment Evaluation (CREATE), included 15 570 patients with ST-segment elevation or new left bundle-branch block. From July 2001 to July 2004, patients received reviparin (N = 7 780) or placebo (N = 7 790) subcutaneously twice daily for 7 days.

The researchers found that the primary composite outcome was significantly reduced from 11.0% of patients in the placebo group to 9.6% in the reviparin group, a 13% lowered risk. These benefits persisted at 30 days.

Reviparin treatment was significantly better when it was initiated very early after symptom onset at 7 days.

Reviparin is considerably less expensive than other antithrombotic agents, such as bivalirudin, and can be given subcutaneously. It could be used in both developed and developing countries.

Source: *JAMA* 2005; **293:** 427-436. Available post-embargo at **jama.com**

Update on antimalarial drug supply

On 8 November 2004 the World Health Organization (WHO) announced a shortfall of artemether-lumefantrine, an artemisinin-based combination therapy (ACT) used to treat malaria.

Based on information provided recently to WHO by Novartis, the shortage is expected to continue after March 2005 because of a continued lack of raw materials needed to make this medicine.

ACTs are currently the most effective medicines available to treat falciparum malaria – the deadliest form of the disease; and artemether-lumefantrine is the only such drug currently available combined in a single tablet.

Novartis has announced that it has secured artemisinin derivatives in quantities sufficient to produce approximately 60 million average treatment courses . However, because most deliveries of raw materials to Novartis will occur in the second half of the year, the company estimates that approximately 30 million treatments will be produced in 2005, and half that quantity will be produced during the last quarter of the year.

These 30 million doses represent about half the amount WHO expects will be needed to meet public sector demand in 2005.

Source: **http://mosquito.who.int/malariacontrol**

UCI researchers create new technique for speeding development of vaccines against infectious diseases

A new technique devised by University of California at Irvine (UCI) researchers can greatly facilitate the development of vaccines against infectious diseases such as smallpox, malaria and tuberculosis. Because the new technique can synthesise a large number of proteins very quickly, it has potential to accelerate vaccine development, particularly crucial in the fight against bioterrorism.

The technique is based on polymerase chain reaction (PCR) and enables the rapid discovery of antigens for vaccines by allowing hundreds of proteins to be processed simultaneously using ordinary laboratory procedures. This new method allows the expression of 384 individual genes from a micro-organism in just one week. Traditional methods take weeks to produce one protein at a time.

The researchers describe their technique in the *Proceedings of the National Academy of Sciences* of 18 January 2005.

'Technologies today are not able to quickly process large amounts of data that arrive in the form of genome sequences from many human pathogens,' said D Huw Davies, lead author of the paper and associate project scientist in UCI's Center for Virus Research. 'Our technique addresses and removes this bottleneck. Remarkably, in only ten weeks, we can make every protein of an organism such as the tuberculosis bacterium – which has 3 900 genes.'

Scientists currently consider developing a safe vaccine to be the best way to blunt a bioterrorism threat against smallpox and other dangerous organisms that terrorists can use as weapons.

'The existing live-virus vaccine against smallpox produces unacceptable side-effects such as allergic reactions, sores, heart inflammation and angina,' said Philip Felgner, principal investigator of the research project and director of the proteomics laboratory within the Center for Virus Research. 'For a vaccine to be an effective defence against bioterrorism, however, it needs also to be safe. With our method, researchers can arrive very quickly at good vaccine candidates that are also extremely safe.'