

old law, recombinant plasmids and other genetically modified research materials could not be exported outside European Union (EU) countries. Taken to its logical limit this meant that a patient who had undergone gene therapy was barred from leaving the EU. International exchange of altered DNA is now permitted without restriction.

Public hearings on deliberate release experiments used to degenerate into media circus and gave environmental groups ample opportunity to hinder the approval process. Last spring in the northern town of Einbeck, for example, some 20 campaigners turned up at a hearing dressed as giant sugarbeets and occupied test sites to protest the planned release of recombinant plants. The protesters were greatly outnumbered by journalists,

guaranteeing extensive media coverage.

The potential loss of such forums under the new streamlined approval process has not gone down well among environmentalists. Beatrix Tappeser of the Öko-Institut, an influential environmental think tank in Freiburg, declares the measures a "sad example of the demolition of civil rights" and charges that potentially dangerous experiments will now go ahead without any public scrutiny. But Secretary of Health Horst Seehofer rejects that accusation. "Show-events by professional demonstrators will be avoided in the future," he says, emphasizing that the existing high-security standards in Germany's laboratories will remain unchanged.

The new law will ease the weight of bu-

reaucracy at one level, but researchers still have to contend with the authorities in Germany's 16 states, where most of the decision-making takes place. The state governments have widely differing levels of enthusiasm for genetic research. "If the state authorities want to extend the procedure, there are a million ways to do so," cautions Willi Siller, biological safety officer at the University of Heidelberg. But geneticists may not have to wait long for this extra hurdle to be removed: The health ministry is now drawing up new guidelines to address the problem, which will be voted on by the state assemblies in the late spring.

—Michael Simm

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META-ANALYSIS

A Hearty Endorsement for Aspirin

Aspirin is one of the world's most widely used drugs, but a major study being published this week suggests it is not used widely enough. If everybody known to be at high risk of vascular disease were to take half an aspirin a day, about 100,000 deaths and 200,000 nonfatal heart attacks and strokes could be avoided worldwide each year, the study indicates. "This is one of the most cost-effective drug interventions one could have in developed countries," says Oxford University epidemiologist Richard Peto, one of the coordinators of the study, a statistical overview, or meta-analysis, of clinical trials in which aspirin was used to prevent blood clots.

It has long been known that aspirin helps prevent blood clots by blocking one of the enzymes that cause platelets to aggregate, and many studies have shown that the drug can reduce the incidence of heart attacks and strokes. But until now there has been no consensus on which patients should receive such treatment and when. Some studies indicate that aspirin reduces stroke only in men; others have suggested that it does nothing for diabetics; and the rare side-effect of cerebral hemorrhage has led some researchers to argue against its use in vascular disease sufferers who have high blood pressure.

This lack of consensus has led to patchy use of antiplatelet drugs: A 1993 study, for instance, found that only 60% of acute heart attack patients in U.S. academic centers were getting such therapy. Says epidemiologist Charles Hennekens of Harvard Medical School: "We need wider indications for the use of aspirin. We need it in women, in hypertensives.... We need to get

FDA [the U.S. Food and Drug Administration] to act to influence doctors."

The new meta-analysis, which covers both aspirin and more expensive antiplatelet drugs, combined the results of 300 trials involving 140,000 patients. Its recommendation: A regime of half a tablet of aspirin a day is valuable for all victims of heart attack and stroke, and other at-risk patients such as angina sufferers and recipients of coronary bypass grafts (see table). "It's not complicated," says Peto. The full analysis will be published in three consecutive issues of the *British Medical Journal* beginning on 8 January.

While the results are likely to bring consensus to the field, there are still a few areas of uncertainty. One major disagreement surrounds the study's finding that aspirin can reduce thrombosis in patients immobilized by surgery, where some of the studies were not double-blinded, and therefore could be biased. Worried about this possibility, thrombosis expert Anthonie Lensing of Amsterdam's Academic Medical Center and cardiovascular clinicians Jack Hirsch and Mike Gent of McMaster University in Hamilton, Ontario, have reanalyzed a smaller set of

data. They included only results of trials that had faultless methodology and looked separately at patients in general surgery and those who had had procedures such as hip replacements, where the surgery itself can damage veins in the leg and further increase the risk of thrombosis. Their conclusion: Aspirin is beneficial only following orthopedic surgery.

Oxford cardiologist Rory Collins, another coordinator of the study, counters that splitting the data into such small chunks defeats the object of conducting a meta-analysis of many trials. And he notes that if the data for general and orthopedic surgery are considered together, there is still a significant benefit from aspirin, even if methodologically suspect trials are excluded.

Another key question, which the overview does not claim to answer, is whether generally healthy people should take aspirin to prevent vascular disease. But the answer may not be too long in coming: 40,000 U.S. female health care workers are now involved in a trial to test the effectiveness of aspirin in the primary prevention of vascular disease.

Peto stresses, however, that such future concerns should not deflect attention from the urgent need for wider use of aspirin now among people at high risk of vascular disease.

Collins, Peto, and Hennekens have already urged the FDA to extend its guidelines on the use of aspirin against vascular disease. The FDA currently recommends antiplatelet therapy only for sufferers of unstable angina, as a measure to reduce secondary heart attacks after an initial coronary, and to reduce secondary strokes in men, but not women. Concludes Peto: "It's time for doctors to look at this evidence and really change their practice."

—Peter Aldhous

SUMMARY OF RESULTS OF ASPIRIN TRIALS				Proportion who suffered nonfatal stroke, nonfatal heart attack, or death during the trial	
Type of patient	Length of treatment	Number of patients	Treatment group	Control group	
Suspected acute heart attack	1 month	20,000	10%	14%	
Previous history of heart attack	2 years	20,000	13%	17%	
Previous history of stroke	3 years	10,000	18%	22%	
Other vascular diseases	1 year	20,000	7%	9%	