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The limits of sharing

President Clinton's offer to share missile defence with his allies brings to mind his presidency's weaknesses — his fondness of fudge and reluctance to embrace unpopular truths.

European leaders have been muted in their public responses to President Bill Clinton's offer, made in Lisbon last week, to share US missile defence technology with "other civilized nations". If this offer was meant to help bridge the growing chasm between European and American perceptions of the missile defence issue, it richly deserved to fail.

Reports that the United States has developed a working technology for national missile defence are grossly exaggerated. Sixty billion dollars have been spent since President Ronald Reagan first proposed such a system, but little real progress has been made. Space-based laser weapons and other fantasies have been jettisoned, and the Ballistic Missile Defense Organization (BMDO) at the Pentagon confines itself to the problem of intercepting a rocket by launching a mechanical interceptor in its path.

Despite this, Reagan's Star Wars fantasy has, since its early days, been accepted by a large part of the US population. People like to believe that American science and technology can solve any problem, and the Star Wars idea was a political success for Reagan. The fact that his vision has been technically discredited, and that tens of billions of dollars were spent with precious little to show for them, hasn't much diminished the political potency of missile defence.

So Reagan's heirs continue to pursue it. In its pursuit, they have even summoned up a category of enemy never previously encountered in the history of warfare — the 'rogue nation', whose leaders are not subject to the logic of intimidation. Opinion polls in the United States show a craving for national missile defence, and that many believe it works and even that it is actually already in place.

Last year, Clinton therefore found it politically necessary to declare that he would decide this summer whether to deploy a national missile defence system. The system would be the fruits of the BMDO, which spends 70% of its $3 billion budget on battlefield defences, 20% on national missile defence and just 10% on technology development. Its technology development plan (see http://www.acq.osd.mil/bmdo/bmdolink/html/tech.html) confirms that the Star Wars dreams have been shelved. There is no real research any more, just a clumsy interceptor system that BMDO engineers are struggling to operate.

The first two formal tests of this system have been unsatisfactory: there are convincing allegations, not adequately refuted, that their results were rigged. Scientific experts in the United States have denounced the system as unworkable (see *Nature* **404,** 799; 2000). A third test, due next month, will not change that picture. The pressure to deploy now, ahead of November's election, is purely political.

Europe's tactfully restrained response to this unedifying shambles seems appropriate. Clinton's failure to convince Western Europe and Russia to collaborate gives the United States an opportunity to re-examine its rush to deploy a national missile defence system. ■

Gene therapy's trials

One major laboratory has closed because of a clinical trial's tragic outcome. But others need publicly to review their roles.

When Jesse Gelsinger, an 18-year-old Arizona man, died during a gene-therapy experiment last autumn, the scientific community first rallied to find out what went wrong. Then politicians and bureaucrats started looking for someone to blame.

Fault has come to rest on the University of Pennsylvania's Institute for Human Gene Therapy (IHGT), whose clinical-trials programme has now been terminated. The IHGT had failed to inform the US Food and Drug Administration (FDA) of adverse events experienced by other patients treated before Gelsinger, according to an FDA letter to the university. But other institutions, agencies and individuals may share some moral culpability: when oversight breaks down, everyone involved in it must examine their role.

The sense that this process is far from settled emerged at a recent Senate hearing. When officials from the Department of Health and Human Services, National Institutes of Health (NIH) and FDA were asked whether recommendations made in 1998 about clinical-trial oversight had been implemented, none responded definitively. Weeks earlier, the health department's Office of Inspector General pointed out that the 1998 recommendations had been largely ignored. Those recommendations spoke directly to many of the problem areas in the Gelsinger trial: informed consent, adverse-events reporting and clinical-trial oversight. The agencies' failure to address issues raised years earlier may have indirectly contributed to the trial's tragic outcome.

Adverse-events reporting may be the clearest example of this. Hundreds of previously unreported adverse events poured in to the NIH once it asked for them following Gelsinger's death. Many gene-therapy researchers privately object to filing adverse-events reports either to the FDA, where they remain confidential, or to the NIH, where they are made public. But, in retrospect, having more public records on adverse events associated with the vector used in Gelsinger's trial would have been useful. Perhaps if enough data on immune responses associated with the vector had been made public before his death, rather than after, the trial would never have been launched.

So whose fault is it that many gene-therapy investigators didn't report their adverse events earlier? The answer is hard to determine, but the NIH leadership may have sent an inadvertent message that reporting to the Recombinant DNA Advisory Committee (RAC) isn't compulsory when in 1996 they tried to reduce the committee's scope.

And although IHGT investigators didn't notify the FDA of all adverse events immediately, they did notify them of similar immune responses. In each case, the FDA let the trial resume. The IHGT and FDA changed the route of vector administration, from intravenously to directly into patients' livers, without notifying the RAC. While that adjustment was intended to limit the vector to the liver, Gelsinger's autopsy showed that it had the opposite effect.

Clearly, the IHGT's closure does not obviate the need for other institutions, agencies and individuals to assess their roles in the tragedy and to make their conclusions public. ■