1. Calleja, C., Pascussi, J. M., Mani, J.C., Maurel, P. & Vilarem, M.J. The antibiotic rifampicin is a nonsteroidal ligand and activator of the human glucocorticoid receptor. *Nature Med*. **4**, 92–96 (1998).
2. Blanchard, J.S. The ying and yang of rifampicin. *Nature Med*. **4**, 14–15 (1998).
3. Nakai, Y. *et al*. Molecular mechanisms of clucocorticoid inhibition of human proopiomelanocortin gene transcription. *J. Steroid Biochem. Mol. Biol*. **40**, 301–306 (1991).
4. Barwick, J.L. *et al*. Trans-species gene transfer for analysis of clucocorticoid-inducible transcriptional activitation of transiently expresed human CYP3A4 and rabbit CYP3A6 in primary ultures of adult rat and rabbit hepatocytes. *Mol. Pharmacol*. **50**, 10–16 (1996).
5. Pichard, L. *et al*. Cyclosporin a druf interactions. Screening for inducers and inhibitors of cytochrome P450 (cyclosporin A oxidase) in primary cultures of human hepatocyes and in liver microsomes. *Drug Met. Diaposition*. **18**, 595–606 (1990).
6. Shuetz, E.G., Schinkel, A.H., Relling, M.V. & Schuetz, J.D. P-glycoprotein: A major determinant of rifampicin-inducible expression of cytochrome P450A in mice and humans. *Proc. Natl. Acad. Sci. USA* **93**, 4001–4005 (1996).

Clarifying AIDS vaccine trial guidelines

In your news article on the recent Geneva meeting to discuss ethical guidelines for AIDS vaccine trials, Adrian Ivinson concluded that a "hard-won consensus" was reached. He also cited an article about the meeting that I wrote for *Science*, in which I reported precisely the opposite conclusion.

I well understand why Ivinson believed that a consensus had taken place—it was a confusing issue for many of the participants, some of whom may not have understood the nuances of the wordsmithing that took place. But I tape recorded the meeting and I think it was his otherwise accurate article that missed the point. Because the interpretation of what happened at the meeting could have significant ramifications, I think it's worth spelling out my evidence.

As we both reported, the contentious debate centered on current ethical guidelines that imply that people who become infected with HIV during an AIDS vaccine trial should, regardless of whether they live in a poor or rich country, receive the best proven treatment. The majority of attendees believed that the guidelines should be modified to read the "highest practically attainable standard.'' But a vocal minority would not compromise on this point, contending that all humans should be treated the same, regardless of where they live.

Near the meeting's end, Ruth Macklin did not record in the minutes, as Ivinson reported, "the consensus opinion that the guidelines should call for the 'highest practical standard'...but would stop short of demanding 'the best proven treatment.'" Macklin explicitly stated that "we did not reach agreement between those two, and therefore there was substantial disagreement." I believe confusion occurred because she did say that the group had reached consensus "on a procedural solution to the very sticky [question]."

Macklin a few minutes earlier had defined what she meant by a procedural solution. "When people disagree or are morally ambivalent, a solution is to turn it to a procedural solution, that is to say who should decide this question. We in this room are unable to decide it....But we do know that there is a procedural solution, and it's precisely the one you just named: This should be left to each country in which the trials are to be conducted. That answers the question of who should decide but it doesn't come close to answering what should be available."

At that point, Christine Grady, an ethicist who wrote *The Search for an AIDS Vaccine: Ethical Issues in the Development and Testing of a Preventive HIV Vaccine*, said, "How is that different?" Grady's point was that some people in the room did not think each country should be allowed to decide this question. Rather, they insisted that there be one standard for the world. From my interviews with these dissenters, I think the suggestion that they changed their thinking at the elenventh hour, as Ivinson's article implies, is inaccurate. And if their objections remained, then a substantial disagreement, not a consensus, prevailed.

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Ivinson replies—I am grateful for Jon Cohen's clarification. It is indeed an important issue and as such clarity is important. Cohen agrees that a consensus was reached but disagrees with respect to what that consensus applied to. Ruth Macklin has told *Nature Medicine* that despite the absence of formal minutes, immediately following the meeting "an official procedural agreement [was] recorded". This read: "... Differences of opinion on whether the standards of counselling (sic) and treatment for trial participants who contract HIV should be those of the sponsoring country or those of the host country were resolved by consensus in favour (sic) of 'the highest practically attainable standard' (which could be arrived at through a fully collaborative decision of the sponsoring and host partners)."

However, in the weeks following the meeting, Macklin tells us, discussions between a few of the meeting's participants (likely including some of the "dissenters" to whom Cohen refers) resulted in this paragraph being amended to read:

"... However, participants in the Geneva meeting did not succeed in reaching consensus on what level of treatment should be provided to participants in a vaccine trial who become infected during the trial. Some people at the meeting argued that the 'best proven therapy' should be provided, in compliance with the current CIOMS international guidelines. Others at the meeting argued in favor of what they believe to be a more realistic standard—'the highest practically attainable' level of treatment. No amount of further discussion brought these two different opinions closer together. Rather than leave the matter entirely unresolved, participants agreed to set aside for the present any attempt to set a substantive standard, and agreed instead on a 'procedural' solution. That solution is to leave decisions about the level of care to the host country in a vaccine trial, those decisions to be made in full collaboration with sponsors of the trial. The result is that different countries will almost certainly decide upon different standards to apply to their own situation. However, in no case may the host country and the sponsor decide on a level of care that is lower than the 'highest practically attainable' level."

Wordsmithing aside, what this tells us is that whereas a change in wording, to date discussed by only a minority of the attendees, has seemingly facilitated broader agreement, the intention remains that trial participants be guaranteed access to the "highest practically attainable standard of care" in the host country while leaving open the issue of whether they should be offered "the best proven treatment". It is this consensus (procedural or otherwise) that I reported.

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Editor