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THE FIRST WORD

CANARY IN A COAL MINE

jehovah buried, satan dead
do fearers worship much and quick
–e.e. cummings

A little while back, movie director Steven Spielberg was talking to a colleague about the latter's newly finished, $25-million movie. "What?" Spielberg said, "You're still doing low-budget pictures?"

This is the age of the blockbuster: the blockbuster movie, the blockbuster play, the blockbuster book, and the blockbuster drug. No others need apply. The mass market is finely attuned to the mega-hit. The system demands big hits to bring in the big money needed to make the big hits. It is addicted, habituated, utterly dependent on the hypertrophic spiral. Its metabolism is so delicately adjusted to high throughput and optimal cost-benefit ratios that it chokes on the less digested, less homogenized, less expensive roughage of more modest expectation. It has evolved efficiency at the expense of flexibility and robustness.

Though fascinating in a spectacular way, it is the kind of overspecialization that did in the apatosaur and baluchitherium.

Which brings us to the U.S. Orphan Drug Act, a measure intended to secure niche treatments for narrow indications and thus counteract the fulminating elephantiasis of drug-development economics.

At the end of February, the President's Council on Competitiveness released its *Report on National Biotechnology Policy*, a 32-page statement of the U.S. Administration's good intentions towards biotech-based industries. (The name of Vice President Dan Quayle, the Council's chairman, is so tightly linked to the report that we must confess to wondering, ungenerously, whether the high-level attention is supposed to reflect biotechnology's importance, or whether the Administration is trying to rehabilitate–or habilitate–a political liability by displaying the Vice President as a serious thinker on difficult topics.) The report does have considerable symbolic importance. It is also sensible, in the unsurprising way conventional wisdom is sensible. Omitting the obligatory political qualifiers and escape hatches, the recommendations are very favorable indeed to commercial applications of the biotechnologies...*if*, of course, they are accepted, and *if* they find expression in agency policies and budget appropriations. (See Jeffrey Fox's "Quayle Likes Biotech, Not Regulation" in this issue.)

The most concrete of the report's recommendations is this: The Bush Administration should oppose any attempt to legislate changes in the Orphan Drug Act. That, too, is sensible. The Orphan Drug Act is the canary in the coal mine–the warning sign, the small creature most likely to succumb to poisonous gas seeping out of the ground. In this case, the poisonous gas is criticism: the Act, it seems, has succeeded too well. Critics accuse biotech companies of camouflaging their products as "pseudo-orphans" by applying for different approvals for different indications.

This isn't manipulation: It's the wave of the future. We have often said that the deepening insight offered by biotechnology will force us to subdivide disease indications according to narrow molecular criteria. And drug-makers will file for approvals on those indications because that is what FDA and good medical practice will demand. The trend will–and should–continue . . . for biotechnology drugs most of all. The current generation of therapeutics derived from broad-acting biological response modifiers and growth factors are inherently broad-spectrum in ways that no other drugs (except possibly aspirin) have ever been. Careful evaluation of indications and regimens is essential.

It is unclear how much competition these strait niches can support–especially when the competitors are expensive-to-develop, expensive-to-produce proteins. Critics say, too, that Orphan Drug status for many biotech drugs is often little more than a ruse–a way of securing market exclusivity while cashing in on off-label applications. Certainly some of this will happen. How much, is hard to say: Remember how much biopharmaceuticals can cost, and how reluctant third-party payers can be when it comes to paying for unapproved procedures.

It would be short-sighted and foolish to scrap or hobble the Orphan Drug program when, in the not too distant future, the majority of drugs could conceivably be Orphans.

–Douglas McCormick