1992 onward, the difference since 1995 being in the detail that science is a smaller part of a larger portfolio in the Cabinet Minister with responsibility for it, and a junior Minister is correspondingly more important.

Finally, and getting into real Whitehall arcana, Ian Taylor was a junior junior Minister (Parliamentary Under Secretary of State), while John Battle is a senior junior Minister (Minister of State).

Obviously much of this is too detailed for the short piece that appeared. But it simply is wrong to suggest that Mrs. Beckett will be doing something new in speaking for science, across all departments, in Cabinet. At the same time, it is great that she looks forward to this important role.

Robert May
Chief Science Adviser,
U.K. Office of Science and Technology,
Albany House, 94-98 Petty France,
London SW1H 9ST, United Kindgom

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Drug Development

Silvio Garattini asserts in his 17 January editorial "Financial interests constrain drug development" (p. 287) that the pharmaceutical industry "is interested in treating the largest possible number of patients with a particular drug." This is untrue. We commit to improving the health of as many patients as possible with a particular drug. This goal necessitates treating a number of sick people with a particular drug even though some do not respond, because the technology to identify responders is a priori not available.

This may change soon as the ability to stratify phenotypes (historically a somewhat imprecise science) is enhanced by genotyping (a highly quantitative and exact science). To advance this goal, we and other pharmaceutical companies are conducting clinical trials to correlate the response to various developmental drugs not only with a patient's phenotype (such as blood pressure) but also with his or her genotype.

Garattini cites the problem of drug resistance and argues that the development of drugs to decrease resistance "is constrained by those drugs' potentially limited market." Pfizer has large programs committed to study bacterial and fungal mechanisms of resistance, and we have recently invested several million dollars with biotechnology companies such as Microcide and Chemgenics to expedite this research. Glaxo Wellcome, in concert with its affiliate Affymetrix, is analyzing viral DNA from patients infected with human immunodeficiency virus to determine which viral genotypes are sensitive or resistant to existing AIDS therapies. This expensive, long-term investment will help physicians select appropriate drugs and may also elucidate mechanisms of viral resistance.

Garattini asks for "[s]pecial collaborative programs linking industry, governments, and academic or scientific institutions." The funding by the U.S. National Institutes of Health of Johns Hopkins University's genotyping center will make this information available to the whole industry and also facilitate the understanding of genetic differences between phenotypically similar disease sites.

Ian Williams
Group Director, Molecular Sciences,
Pfizer Central Research,
Groton, CT 06340, USA

Response: Williams defends the position of the pharmaceutical industry, which I did not intend to attack in my editorial. I simply tried to explain that many orphan areas in medicine cannot be taken care of by industry although these areas are of great importance for patients and national health services. I certainly know of and appreciate the activity of the U.S. National Institutes of Health and Johns Hopkins University, but my aim was to suggest extension of such activity in Europe and through an ad hoc agency.

Silvio Garattini
Director, Instituto di Richerche
Farmacologiche "Mario Negri,"
Milano 20157, Italy

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Endosomal Targeting and the Cytoplasmic Tail of Membrane Immunoglobulin: Retraction

In our report (*1*) "Endosomal targeting by the cytoplasmic tail of membrane immunoglobulin" (18 Apr., p. 407), we measured the production of interleukin-2 (IL-2) with an MTT assay (*2*). Recently, we repeated our experiments with another assay for measuring the production of IL-2, namely, thymidine incorporation in the cytotoxic T lymphocyte cell line CTLL-2. In this system, differences between results from positive and negative control are severalfold higher than they are with the MTT assay. This reexamination, together with the analysis of additional clones, revealed problems with the sensitivity and calibration of our MTT readout that jeopardize the conclusions of our study (*1*), because the different transfectants no longer fell into the clear pattern presented in our report. Although the γ2am cytoplasmic tail of membrane-bound immunoglobulin may have a role in antigen presentation, our data do not allow us at this stage to establish this role.