

The Cost of Developing Imaging Agents for Routine Clinical Use

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Abstract: The objective of this study was to estimate the financial cost of developing new imaging agents for clinical use and to discuss the effects of these costs on the future clinical imaging agent environment. Publicly available financial data from the annual reports of major companies developing and selling imaging agents were examined and the data used to develop cost estimates. These estimates were compared with the in-depth data and analyses available for the development costs of therapeutic drugs. The cost of developing a drug for diagnostic imaging to commercialization is in the \$100 to \$200 million range, whereas a blockbuster imaging drug has current sales of \$200 to \$400 million. Most of these blockbuster imaging agents have been on the market for some time. The majority provide morphologic images with general indications in a slowly changing section of the market. Future agents will most likely address smaller markets and be in the rapidly developing molecular imaging field. The costs are high and are a significant brake on the development of imaging agents for commercialization. If new imaging agents are to realize their commercial potential, ways must be found to make the financials more attractive. The prices per dose are currently low so they must either be greatly increased for new imaging agents, with a corresponding increase in the value of the information they provide, or the use of imaging agents must be widened and/or their development made less costly in time and money. Without addressing these issues, the commercialization of new imaging agents will continue to be slow and may get slower. This will impact the progress of imaging agents toward use as validated biomarkers.

Key Words: costs, imaging agent, biomarker, development

(*Invest Radiol* 2006;41: 206–212)

The submission of new chemical entities (NCEs) to the regulatory authorities for approval as *in vivo* imaging agents has, like submissions for therapeutic agents, not kept pace with the explosive generation of basic biologic data, which many expected to yield a flood of new drugs. As with

the therapeutic agents, although increased funds are being spent, this has not led to increased submissions or approvals of imaging agents. The increased funds expended on developing imaging agents have been channeled in part to pay for the increased cost of bringing an NCE to the market. The development costs for diagnostic imaging agents have increased in the same way as have those for therapeutic drugs. However, although the development costs of therapeutic drugs are relatively well known, although still controversial, no such data are generally available for imaging agents. The therapeutic pharmaceutical industry consists of many companies that has allowed the collection, analysis, and publication of primary confidential information whilst maintaining the confidentiality of the details.¹ In contrast, there are a limited number of companies that develop imaging agents; thus, one cannot request and use detailed data from the individual companies for use as input for financial models and still maintain confidentiality. As an alternative, the annual reports of major companies developing and selling imaging agents were examined for useful primary information, which was supplemented with data available from other secondary public sources to develop estimates on imaging agent related research and development (R&D) costs, market sizes, etc. These estimates were compared with the more robust estimates for the development costs for therapeutic drugs to establish the validity of various commonly held empirical relationships. These relationships were then applied to the imaging datasets to derive average development costs for an imaging drug.

Therapeutic Drug Sales and Costs

For a nongeneric therapeutic drug, a small/specialty market can be defined as peak year sales of <\$250 million, midlevel \$250 to \$1000 million and large/blockbuster >\$1000 million. The larger pharmaceutical companies expect peak-year drug sales for a blockbuster therapeutic in excess of \$1 billion. These are not as rare as might be expected because the number 10 of the top-selling drugs worldwide in 2003 earned \$3.4 billion.² Global pharmaceutical sales for 2004 were approximately \$520 billion.³

The cost of developing therapeutic drugs has been periodically derived from data provided by drug companies. In one of the most recent derivations,¹ 24 firms from various countries were asked to provide data with 10 finally doing so covering a total of 64 drugs. These data were inserted into a financial model that in various forms is widely used to calculate the expected return on an investment.⁴ The cost of

Received July 21, 2005 and accepted for publication, after revision, October 5, 2005.

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ISSN: 0020-9996/06/4103-0206

developing the 64 drugs to the approval stage was calculated to be \$802 million in year 2000 dollars.¹ This cost has been challenged as being too high (should be \$150 million)⁵ or too low (should be \$1700 million).⁶ The disagreements tend to center on the details of the financial model, and both the lower and higher proponents have clear, vested interests in their positions.

Turning to more empirical methods, the cost of developing new drugs can also be derived from the yearly amount spent on R&D (the range for 2004 is 9–25% of sales with the average being approximately 16%) divided by the number of NCE approvals or significant new indications in a given year. Dimasi et al¹ have performed the calculation on an industry-wide basis and obtained values of \$1000 million for the year 2000 and an average of approximately \$730 million for the previous seven years. Selecting three quite different types of major pharmaceutical companies and using R&D costs and NCE/major indication approval figures available in their 2004 monthly reports (crosschecked with other sources but a figure open to interpretation), one can estimate it cost Abbott approximately \$1003 million,⁷ GSK approximately \$830 million,⁸ and Genentech approximately \$475 million⁹ per NCE or major new indication (Table 1).

Finally, a common rule of thumb used to evaluate the expected value of a drug is that peak-year sales should equal or exceed expected development costs and this is roughly supported by the existing numbers. Thus, if peak-year sales of a second-tier (not top 10) blockbuster drug of ~\$1 billion are expected, one would expect development costs of a similar order and would be encouraged to move ahead with development.

So, whether one derives figures using detailed financial models or the various empiric methods, the cost of developing a therapeutic drug appears to be in the region of \$850 million.

Imaging Agent Sales and Costs

Annual sales of drugs by Bristol-Myers Squibb (BMS) and Schering AG, two of the few companies that each have both a therapeutic and imaging agent segment, are approximately \$15.4 billion¹⁰ and \$5 billion,¹¹ respectively. BMS has 4 drugs in the large/blockbuster category, but Schering AG has only one. Imaging agent sales are approximately 4% (BMS) and 27% (Schering AG) of total pharmaceutical sales.

The total market for imaging agents is much smaller than that for therapeutic drugs (Table 2). United States sales, which are approximately half that of the total, were \$2.8 billion in 2004.¹² The worldwide figures for 2004 are projections¹³ made in 1999 and are quite accurate except for ultrasound

TABLE 1. Financial and Approval Details of Representative Pharmaceutical Companies for 2004

Company	Pharmaceutical Sales (\$Billion)	R&D as Percent Sales	NCEs/New Indication	Cost per NCE (\$Million)
Abbott	11.6	8.6	1	1000
GSK	31.3	15.9	6	830
Genentech	3.75	25	2	475

TABLE 2. Worldwide or US Total Imaging Agent Sales 1999 and 2004

Modality	US Sales (\$Million) ¹²	Worldwide Sales (\$Million) ¹³	
	Actual 2004	Actual 1999	Predicted 2004
X-ray	964	3480	3354
MRI	342	430	800
Ultrasound	35	40	280
Nuclear	1500	1165	1995
Total	2841	5115	6429

where the predictions were overly optimistic. The total worldwide imaging agent market is just over 1% of the total therapeutic drug market. The total worldwide sales of all x-ray contrast agents if treated as a single drug would just fall into the number two spot of the therapeutic drug rankings in 2003 dollars. The total worldwide imaging agent market is about twice the nondiagnostic sales of Schering AG and about half that of the nondiagnostic sales of BMS. Annual sales of the most successful imaging agents are correspondingly much lower than those of therapeutic drugs.

There are five major imaging agent companies based on imaging agent sales. These are Amersham—now GE, BMS, Bracco, Schering, and Tyco. However, the level of publicly available financial data provided by these companies is variable. Bracco is privately held and little information is available, Tyco does not break out imaging agents as a separate segment in their financial reports, and BMS provides sales figures but not R&D figures. The most complete datasets are only provided by Amersham/GE and Schering; however, these 2 companies do represent almost 50% of the total. This is as good as, if not better, representation of the field than for the analysis of therapeutic drug development costs.

Amersham,¹⁴ Schering,¹⁵ and BMS¹⁶ annual reports for 2003 or 2004 record worldwide sales for a variety of imaging agents (Table 3). Annual sales of the largest selling diagnostic imaging agents barely make it out of the small/specialty category of therapeutic drugs. In addition, most of these drugs are mature and have been approved for some time, and their sales have benefited from extensive postinitial approval efforts.

TABLE 3. Worldwide Sales of Imaging Agents

Product(s)	Modality	Company	Annual Sales (\$Million)
Omnipaque®	X-ray	Amersham (GE)	400
Visipaque®	X-ray	Amersham (GE)	225
Iopamiron®	X-ray	Schering	295 [†]
Ultravist®	X-ray	Schering	290
Magnevist®	MRI	Schering	370
Omniscan®	MRI	Amersham (GE)	195
Myoview®	Nuclear	Amersham (GE)	270
Cardiolite®	Nuclear	BMS	405
FDG®	Nuclear	Multiple*	190 ¹²

*This product is a generic available from multiple sources.

[†]Iopamiron is also sold by Bracco but there are no sales figures available.

The proportion of annual sales that a large company spends on R&D for in vivo imaging agents is smaller than that spent on cold therapeutics and is 6% to 11% of worldwide sales. The absolute value is \$70 to \$150 million based on data from annual reports and is, therefore, much smaller (Table 4). This money is spent on multiple programs that yield, at the most, one NCE approval or new indication worldwide each year.

There are no publicly available figures for the cost of developing imaging agents derived using the formal Tufts procedures, but using the empirical relationships found here for therapeutic drugs of 1 year's costs or peak-year sales, one can come up with a range of \$100 to \$150 million for imaging agents. Epix, a company focused on the development of magnetic resonance imaging agents, reports a total R&D spend from inception to the time their first NDA for MS-325 was filed of \$135 million.¹⁷ They have a second lead, EP2104R, for a different indication, which entered clinical trials in 2004 but with the completion of 18 clinical trials totaling approximately 1500 patient,¹⁸ clearly the majority of these costs were incurred by MS-325. This is supported by data from Epix who in December 2003 reported that to that date (when they filed the NDA), they had spent \$85 million on the development of MS-325 (Peyton Marshall [Chief Financial Officer, Epix] declined to discuss specific financial details about the deal. However, he said the company has spent approximately \$85 million over 8 years in discovery and development efforts associated with MS-325).¹⁹ They also provide a timeframe for development of an imaging agent of greater than 9 years, which is only a little shorter than the 12.9 years of therapeutic drugs.²⁰ The cost of money tied up in this effort is thus comparable. It might be tempting to speculate that there are numbers of small/startup companies that are actively pursuing the development of imaging agents at much less cost on an individual basis. This is a fallacious argument because the costs of such companies, including those that fail, must be added together and divided by the number of NCEs that collectively gain approval either directly or through sale/licensing to established companies. The Epix data show the expenses that a successful (to date) small/startup company incurs.

The yearly worldwide sales of the most successful imaging agents, all of which have been on the market for some time, are in the \$200 to \$400 million range. Most of

these agents image morphology, two are myocardial perfusion agents and only one, FDG, belongs to the currently fashionable molecular imaging agent class of drugs. It is unclear at this time what the business model for new positron emission tomography (PET) agents is because the main market leader (FDG) was developed outside industry, was in experimental use for over 20 years before approval, and the NDA is not held by a single company. Nevertheless, PET agents are being developed by large imaging agent companies.

What is needed to persuade a company to begin development of a new imaging agent today that must achieve peak sales figure in excess of the \$100 to \$200 million range? At the simplistic level, if one sets the upper limit on price at \$1000, approximately 5 times more than the current Centers for Medicare Medicaid Services (CMS) reimbursement levels for FDG in an outpatient setting,²¹ then a given drug company will need 100,000 patients or uses a year. If it is a promising market, then one has to believe that there will be more than one company in the field, so let us double it to 200,000 patients or uses and then let us assume that penetration is 80% (a high number). This gets us to 250,000 patients in the pool. This is already more than the oft-cited expedient of developing an agent as an orphan drug, which brings with it some advantages in exclusivity. The U.S. Orphan Drug Act²² puts limits on the number of persons to whom the drug can be administered to in a year of 200,000. Alternatively, one can imagine a drug with few patients but more uses per year, but this too exceeds the Orphan Drug Act requirements in the instance in which there is no reasonable expectation that costs of research and development of the drug for the indication can be recovered by sales of the drug in the United States. This latter point begs the question of is there anything better for a company to do with its money (or somebody else's) than to recover costs using an orphan drug mechanism?

DISCUSSION

If the price per dose received by an imaging agent company is \$100 the number of units of an imaging agent that must be sold per year to meet the minimum \$100 million development costs is \$100 million/\$100 or 1 million units. It is hard to imagine how a molecular imaging agent might command such a large use because even radiopharmaceutical myocardial perfusion imaging, a mature market with large numbers of patients and more than 1 product, is performed with a total of only approximately 4.5 million procedures each year. Current lowest FDG unit prices of \$200 to \$300 (and it is not clear that this is a real number) are insufficient to meet today's development costs. A price comparable to those cited for FDG only reduces the required patient numbers to approximately 300,000 to 500,000 for a once-a-year imaging agent, and this is the total market assuming 100% penetration and no competition.

Options available to increase revenue are:

- Decrease the cost of bringing a drug to the market
- Charge more for a unit of drug
- Increase use of the drug
- Increase margins

TABLE 4. Annual R&D Spend on Imaging Agents and Percent of Imaging Agent Sales

	1999	2000	2001	2002	2003	2004
Amersham						
R&D costs (£)	74	74	83	95	102	—
% sales*	10	9.5	9	10	10.5	—
Schering						
R&D costs (€)	67	105	121	137	134	125
% sales*	6.4	7.7	8.3	9.7	10.2	9.6

*Sales of imaging and radiotherapy products. Radiotherapy sales are a small percentage of this total. Systemic radiotherapy research, if performed, is included but is a small percentage.

If collectively these options fail to predict acceptable revenues, then the only recourse for a company is to avoid all drugs and markets that cannot be seen to meet the desired levels of sales.

Let us now examine each of these in turn.

Decrease the Cost of Bringing a Drug to the Market

The 3 stages in developing a drug to the NDA stage—discovery, preclinical, and clinical—can be addressed separately.

Discovery and preclinical costs may be less than for cold therapeutic drugs, but as in all therapeutic areas, the companies are already striving for efficiency. One can imagine using the large datasets generated during discovery and preclinical development of therapeutic drugs to select, eg, small molecules that might make useful imaging agents, not the approved drugs themselves because they rarely have the correct characteristics for an imaging agent. Leads originating from such sources are most suited to generating molecular imaging agents. However, big drug companies have in the past been very reluctant to open up their files for such purposes. The National Institutes of Health (NIH) is oft-cited as a source of drugs that commercial pharmaceutical companies bring to the market yet by their own reckoning, NIH has had a significant hand in the development of only 2 classes of compounds that became blockbuster therapeutic drugs.²³ NIH did not have any significant input to the discovery and development of the majority of the imaging agents with large sales, the morphology imaging agents. NIH is more open than the drug companies, but there is still a dearth of potentially commercializable imaging agent leads. Academic institutions performing imaging agent research (frequently, of course, funded by NIH) are a potential source of commercializable leads such as the licensing of Pittsburgh compound B by Amersham (now GE) for Alzheimer's imaging.²⁴ This is similar to the current therapeutic model of large companies supplementing their internal research efforts by buying small companies or licensing their leads, but does it make it less expensive or does it reduce risks at a higher cost? Another model is the collaboration between imaging companies and therapeutic companies such as those between GE and Lilly or Roche.²⁵ Although this will undoubtedly lead to the development of new imaging agents, it remains to be seen if this will also lead to commercialized imaging agents.

Of the \$100+ million that companies spend on developing a diagnostic imaging agent, most is spent during the clinical phase. This is no different from therapeutic drugs. The cost of performing clinical trials varies widely.^{2,26} There are various sources for the cost per patient for each phase and type of trial. Imaging trials may be less expensive than those of therapeutic drugs but if they are to require long follow up, eg, to confirm predictive accuracy, or are for validation as a biomarker, this may not be true. Speed is of the essence because delay increases costs and reduces revenues. Even for a diagnostic drug that might have peak sales of \$100 million a year, a day is worth approximately \$300 thousand in delayed revenues. A delay in killing a drug disproportionately increases costs, and strenuous efforts are being made to kill

candidates as early as possible in the pipeline. Indeed, imaging has been touted as an efficient way of selecting the best among multiple therapeutic candidates in a single phase I trial. Overall, worthwhile savings may only be found in the clinical phases, and there is a need to be able to perform proof of concept studies as efficiently (speed \times cost) as possible as mentioned in the U.S. Food and Drug Administration's Critical Path document.²⁷ The regulatory authorities are making suggestions as to how this might be achieved,^{28,29} but it is too early to say if these restated regulatory positions will materially change the rate of commercialization of new imaging drugs. They may reduce the cost of getting to the proof of concept stage, but they do not remove the fact that for this to occur, there must already have been a decision to develop an imaging agent based on acceptable returns on investment. In addition, although they address some issues for the proof of concept stage, by far, the major cost of clinical trials occurs in phase III for which little resolution of the causes of increasing costs has been found.

Although the major pharmaceutical companies are energetically incorporating imaging into their clinical trials of potential therapeutic agents, it is too early for it to have led to a flood of new potentially commercializable imaging agents. The majority of new imaging agents developed under these circumstances are not well publicized and are frequently very specific and too much a product of the program for which they were developed. Much discussion has occurred on the potential use of imaging agents in personalized medicine as biomarkers,³⁰ but if this is to occur, the thorny financial issue of an additional gatekeeper governing the use of a therapeutic drug must be resolved to the satisfaction of all. Also, the cost of performing the trials necessary for validation of the imaging agent must be assigned as well as a means for the imaging companies to recover the value of such a biomarker from the therapeutic companies that might use it in drug development.

Charge More for a Unit of Drug

For an imaging agent, there is an historical upper limit for the price of a dose and even in the best of circumstances, in which the value of the information gained is very high or unique, there are financial pressures that are limiting. As discussed here, it is most probable that sufficient return cannot be achieved on price alone but will require widespread use as well. There is not the same price restraint for therapeutic drugs in which prices can be more than an order of magnitude higher than the perceived limit for a diagnostic. This is evident in the reimbursement of the recently approved radiolabeled antibodies, Zevalin[®] (Biogen Idec, Cambridge, MA) and Bexxar[®] (GSK; Brentford, Middlesex, U.K.), which is in the range of \$25,000²¹ and which include an imaging agent component in excess of \$2000. Prices of tens of thousands per oncology therapeutic agent are not uncommon for the newer anticancer drugs, but those over a few hundred dollars are rare for imaging agents. Only the antibody-based radiopharmaceuticals (which are mostly the newer drugs) have the opportunity to command increased prices of more than \$1000 per dose.²¹

Increase Use of the Drug

As the return is the sum of both price and volume increasing use is only sufficient of itself at the very highest levels of use, which can be achieved with multiple uses in the same patient as well as with many patients. Each of these opportunities is present in the cardiac imaging market but may not be so in other markets unless the drug is approved for use in patient management—prognosis rather than diagnosis. This, of course, adds a new (expensive) dimension to the clinical trials, especially if the pathologies are narrowly defined. The use of an imaging drug in the clinical phases of the development of a therapeutic drug is not on its own financially viable in the present circumstances unless the imaging agent is already approved for that use or at least marketed. No company would/could afford to commercialize an imaging agent for the drug development market alone, and even additional indications as a surrogate/biomarker have financial and ownership difficulties that have not been resolved, so this aspect of the “opportunity” described in the critical path is still wanting.

The more the pathologies are divided up, “is a target in one cancer the same as the ‘same’ target in another type of cancer?,” the smaller the market for each indication. Each indication must be supported by clinical trial data so additional indications increase costs. Here, the position of the regulatory authorities as to what constitutes a defined clinical setting³¹ is key. At present, it is not clear if the guidance document for imaging has been practically tested in this regard to see if it is sufficiently accommodating.

Increase Margins

The cost of goods of many imaging agents is not the main driver of the overall cost to develop the drug or the final price and in those cases in which it is there is little room for reduction.

Avoid All Drugs and Markets That Cannot Be Seen to Meet the Desired Levels of Sales

Well-established drug companies have a fairly rigorous system in place to screen out ideas for drugs or targets that do not meet the required financial criteria. It is not a foolproof process by any means, but it does set a bar for acceptance. In established imaging companies/divisions, that bar has to be very similar because they all use the same financial methods and positions to determine returns. There will, of course, be differences in the perception of the potential markets, and we all acknowledge that some of the inputs to the financial models are not robust and will change. This means that compounds that work (scientifically) are not being developed and targets that are druggable are not being addressed because the return on investment is perceived to be insufficient or too risky. (Such a screening process is less evident in the academic arena, and reasonable arguments for and against the status quo can be made.) In general, avoidance of low-return drugs is not publicly evident except perhaps in the failure of larger companies to take up potential niche products from smaller/startup companies despite evidence of efficacy.

It is also the practice of drug companies to periodically revisit past decisions (positive or negative) to confirm their

continued relevance, especially in the light of changed circumstances. An example of this is the recent termination by North American Scientific of activities associated with Theus³² who were developing, among other things, the Annexin V-mediated imaging of cancer. The company stated that it was redirecting approximately \$10 million it projected to spend on the Hynic-Annexin V program in fiscal 2005 to other product development opportunities despite the fact that the program continued to yield compelling clinical data. At the time, it reported that it had failed to interest other companies in carrying on the program. Clearly, the return on investment to North American Scientific by placing their resources elsewhere was perceived to be faster/less risky/bigger than for this imaging opportunity. Imaging agent development is definitely vulnerable in mixed-use companies to other opportunities (eg, therapeutic drugs or imaging instrumentation) presenting a greater return on investment unless they can be tied to these other opportunities and collectively increase potential returns.

A new use need not of itself establish a sufficient medical need to justify further commercialization of a new imaging agent as can be realized by examining recent publications on potential new imaging agents. Two papers published in this journal in 2005 present data on new indications for compounds already approved or well down the development pathway. These have less of a hurdle to surmount because much of the development costs have already been justified and consumed by the leading indications; however, the expected return should still justify the (clinical) cost of further development of these particular indications. A paper by Mandry et al³³ presents a new use (renal function imaging) for a compound that is reported to have favorable characteristics versus other gadolinium chelates. However, these are themselves not widely used relative to the well-established laboratory tests and scintigraphic methods and so the medical need for this new agent/indication will probably not stand on its own. There is little chance of being able to charge a premium for this indication but the case pool could be large. Thus, it is unclear if the expected sales would justify the cost of the clinical trials, although the risk of failure is small and the trials themselves relatively simple. A paper by Tsuda et al³⁴ proposes a new indication for Primavist for detecting lymph node metastases, which has already been addressed with some success by, for instance, iron oxide particles, scintigraphy, and, using the blue dye method for breast cancer, by optical imaging methods. The clinical trials here would be more expensive because there is not a well-accepted comparator and so there is the potential for an expensive follow up after surgery. As with the previous compound, it is unclear if the financials would be sufficient to warrant further development costs for this indication. Such studies are frequently needed to increase awareness of an agent or to widen the indications, etc, and the costs need to be apportioned accordingly. Given limited budgets, costs spent here may increase near-term financial returns but reduce longer-term efforts to produce NCEs.

Two additional papers published this year in this journal describe examples of compounds that are more closely

tuned to the potential for providing data useful to the concept of personalized medicine. Simon et al³⁵ describe preclinical data on a new macromolecular iodinated contrast agent that may provide data on the permeability of tumor vessels (and the physiological) response of tumors to therapy. This is an indication with an established medical need based on non-clinical data but which has not been proven in the clinic because of deficiencies in the contrast agents. It would appear to have some potential and be worth pursuing in this regard, although some considerable thought would have to be expended on the most efficacious and efficient clinical trial design. Some of the alternative uses such as angiography may well be obviated by the advancements in multislice CT machines etc. The authors acknowledge that there is some effort to invent magnetic resonance imaging agents able to satisfy the same medical need(s) and present arguments for each. Finally, the paper by Bremer et al³⁶ extends their work of optical imaging with protease sensing probes using the only “molecular imaging” agent of these 4 examples. The considered medical need is reasonable and has perhaps an even greater potential for qualification as a biomarker than simple permeability because it is designed to measure “activity at target.” Again, however, the selection of the indication and the design of the clinical trials will be crucial to the commercial success of such a drug.

CONCLUSIONS

If one accepts that the “simple” CT and magnetic resonance imaging (MRI) agents are so good that there is little room for improvement, we are now in the era of molecular imaging. Now, of course, it is broader than before (when it used to be called nuclear medicine) with the strength of the recent PET market opening up the field, but also with the realization that ultrasound and perhaps light-based imaging agents have the necessary characteristics for in vivo molecular imaging. However, with increased specificity comes narrower markets than exist for the traditional morphology-indicating CT or MRI agents. Also, demonstration of efficacy of specific molecular imaging agents may be more complicated than for a “simple” morphology-depicting contrast agent and may take more time and expense.

However one looks at it, more money is being spent on developing new drugs, but approvals are not keeping up so the cost of developing new drugs, including imaging agents, is increasing. As the empirical relationships between development costs and peak year sales are similar for imaging and therapeutic drugs, it seems unlikely that big drug companies will take on the development of an imaging agent for its own sake when the very biggest imaging drugs hardly make it out of the small/speciality market size group. This leaves it to the smaller companies who may be able to work less expensively (although it is not clear that they have the funds to see a compound through to commercialization) and who may be satisfied with smaller market sizes. However, the numbers published by EPIX Medical do not support much lower costs. PET is a big unknown because it is new to commercialization and there is no existing business model to follow. Because most of the compounds furthest along are in the public

domain, a good financial return is more dependent on technology than basic science. The idealized vision of a new class of imaging drugs providing regional phenotypic information for use in personalized medicine is in jeopardy if the financial constraints to the development of such imaging agents are not worked around.

ACKNOWLEDGMENTS

The author acknowledges many animated discussions with Mike Tweedle and Paolo Bandera the results of which significantly improved the manuscript.

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