

1 lot of other people have thought about as well.

2 The first is the ease or possibility of
3 self-diagnosis, the presence or absence of symptoms
4 which can accurately make the diagnosis -- pain,
5 itching, cold, allergy, and so forth. Related to this
6 is the question of self-diagnosis of other medical
7 conditions which might counter-indicate the use of the
8 drug. That will come up, and I'll mention it briefly
9 in the case of the cholesterol lowering drugs.

10 An example where we intervened in a
11 problem in this category was back in the early
12 Eighties, 1983, I think, where the FDA had decided to
13 switch from prescription to over-the-counter status an
14 asthma drug, metaproterenol, brand name Metapril, and
15 we believed that this was dangerous, because it is not
16 possible for someone to accurately make the diagnosis
17 on their own of asthma.

18 My chief of medicine, Dr. Ramilkamp,
19 taught us that all that wheezes is not asthma.
20 Someone who may be wheezing may have heart failure or,
21 as Dr. Chao mentioned, hypertension, and what may be
22 good for treating asthma may be fatal for treating
23 someone who actually has heart failure as the basis of
24 their wheezing.

25 The second principle is self-limited or

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1 chronic condition. It's related, in a way, to the
2 first principle, because if you have a symptom that
3 you recognize, you treat it and it goes away. It's a
4 self-limited disease or, in some cases, you may have
5 disease that may go away on its own, such as a cold.

6 This is important in terms of the duration
7 of treatment and the evolution of both the change in
8 the course of the disease and the occurrences of
9 adverse reactions or interactions which may require
10 physician monitoring. A long term use such as for
11 diabetes or hypertension or cholesterol lowering is
12 more likely to get into the problem of interactions or
13 adverse reactions than something you use for a shorter
14 period of time.

15 Third, benefit/risk ration and its
16 evaluation: Because the continued benefit/risk
17 evaluation by the patient without any input from the
18 physician is troublesome in a number of areas, you may
19 actually wind up altering the ratio of benefit to
20 risk. What might appear to be a good ratio initially
21 may turn out to be bad. The patient may not be aware
22 of the development of adverse effects or interactions
23 and so forth.

24 So that this whole constant need to
25 evaluate the benefit/risk ratio for chronic diseases,

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1 which I believe a physician or a nurse practitioner
2 needs to be involved in, is something that, I think,
3 for many of these kinds of conditions is beyond what
4 a patient can do.

5 Fourth, low potential for harm which may
6 result from abuse under conditions of widespread
7 availability: This is a quote from the Code of
8 Federal Regulations that has to do with part of the
9 definition of what an over-the-counter drug is.

10 The abuse here does not mean drug abuse as
11 in street abuse. It refers to the kind of abuse that
12 occurs when a patient generally believing that over-
13 the-counter drugs are safer than prescription ones --
14 I think that's something that's been well established
15 and in general is true -- may say, quote, "if one pill
16 does so much good, two or three will do even better;
17 so I'll take more than one."

18 Despite the introduction of most OTC
19 versions of drugs at doses lower than the prescription
20 form, this restriction can be easily overcome because
21 of the history of patients increasing their dose.
22 Related to this is the question of whether the
23 potential for harm is such that the use of the drug
24 without the involvement of the physician or other
25 learned intermediary such as a pharmacist is not

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1 appropriate.

2 The switch of drugs with a low margin of
3 safety, ones where doubling of dose may significantly
4 increase the toxicity, should be generally opposed.

5 Fifth, number of adverse reactions of
6 interactions and the ease of detecting them: If there
7 are numerous adverse reactions or interactions, as Dr.
8 Chao referred to, which may not be fully known to the
9 patient or the physician, there's even more cause for
10 concern than the already troublesome situation
11 involving only prescription drugs, and in this case
12 the physician who is prescribing prescription drugs,
13 but the patient is possibly, unbeknownst to the
14 physician, taking over-the-counter drugs.

15 If the detection of the adverse reaction
16 is hampered by the absence of signs which the patient
17 can detect, such as abnormal laboratory tests which
18 are an early signal of liver toxicity, the frequent
19 absence of the physician's involvement because the
20 drug is available OTC may be dangerous.

21 Six, long term data from prescription use
22 to assess likelihood of problems with OTC use:
23 Needless to say, if the drug has been available for a
24 long time on a prescription basis, we're going to know
25 more about it, and drugs that have only been around

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1 for a few years, probably just on that basis alone,
2 should not be switched.

3 Seven, toxicity compared with other drugs
4 in the class: If there are other drugs in the class,
5 how does the safety and benefit/risk ratio compare to
6 these? A good example of this was the rumors started
7 by, I'm sure, partly the pharmaceutical company
8 involved of the possible switch of Pyroxycom or
9 Feldene from prescription to over-the-counter status.

10 There is little question from a large
11 number of case controlled studies that the
12 gastrointestinal toxicity with this drug is
13 significantly more than with Ibuprofen or with
14 Naprosyn or with other already switched analgesics or
15 drugs for treating arthritis.

16 So that, even within a class where it may
17 make sense to switch some members, it doesn't make
18 sense to switch others.

19 I'm just going to finish the few minutes
20 I have left with specific concerns about switching
21 cholesterol lowering drugs, partly in anticipation of
22 the hearing next month; but I will give much more
23 detail on why we are opposed then, but because I think
24 that it's a good way of looking at a number of the
25 other classes.

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1 We go back to some of these same
2 principles: Ease or possibility of self-diagnosis.
3 Given that the indications for these drugs in the OTC
4 status would be a total cholesterol level between 200
5 and 240, an LDL of over 130 milligrams per dl, and the
6 absence of established cardiovascular disease or
7 diabetes, it is highly unlikely that this combination
8 of evidence plus other information that should be
9 there will be present before the OTC purchase of
10 Mevacor or Prevacol.

11 Since the indication for these drugs
12 varies as a function of other risk factors, this
13 overly simplified indication by total and LDL
14 cholesterol is, at the least, misleading. The
15 National Cholesterol Education Program guidelines
16 state, for example, that those without established
17 cardiovascular disease or only one other risk factor,
18 such as smoking or hypertension, should start
19 cholesterol lowering drugs only if their LDL is over
20 190, not 130. Even with two other risk factors, the
21 recommendation is 160 or over.

22 This is in contrast to the company's
23 proposed recommendations of starting drugs for levels
24 of over 130, as announced in the notice of the July
25 meeting.

1 In addition to the problem of accurate
2 ascertainment of cholesterol levels, the warning
3 against use in people with established cardiovascular
4 disease or diabetes belies the fact that many people
5 with these diseases have not yet been diagnosed.
6 Thus, self-diagnosis of these conditions is not a
7 reality unless the patient had previously had a heart
8 attack or angina or symptoms of diabetes that led to
9 a diagnosis.

10 Self-limited or chronic condition:
11 Because of the implications of an increased risk of
12 cardiovascular disease associated with elevated
13 cholesterol levels, the use of these drugs could well
14 be on a chronic basis or forever. In addition to the
15 need for a physician evaluation initially, medical
16 follow-up is also necessary for the detection of
17 either an evolution into cardiovascular disease and/or
18 the occurrence of adverse reactions or interactions
19 with other drugs which may require physician
20 monitoring.

21 Finally on this issue, number of adverse
22 drug reactions or interactions and ease of detecting
23 them: An additional problem with Mevacor and Pravacol
24 concerns the impossibility of self-diagnosis of an
25 early sign of liver toxicity, namely the presence of

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1 elevated liver enzymes in a blood test.

2 At the earliest stages this is completely
3 asymptomatic and can only be detected with regular
4 monitoring under the supervision of a physician or
5 other health professional such as a nurse
6 practitioner. The current physician labeling for
7 Mevacor states, quote, "Persistent increases to more
8 than three times the upper limit of normal in serum
9 transaminases, a liver function test, occur in 1.9
10 percent of adult patients who receive Lovastatin for
11 at least one year."

12 It goes on to say that usually, but not
13 always, these go back to normal. Because of this,
14 labeling further states, quote, "It is recommended
15 that liver function tests be performed before the
16 initiation of treatment, at six and 12 weeks after
17 initiation of therapy or elevation of dose, and
18 periodically."

19 There is a similar warning on the labeling
20 for Pravacol. The need for this kind of surveillance
21 is not consistent with a switch to OTC status of these
22 or any similar drugs.

23 Common to the concerns of switching
24 cholesterol lowering drugs, diabetes drugs and drugs
25 for hypertension are many of the same kinds of

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1 concepts. All are used to treat lab values,
2 cholesterol, blood sugar, elevated blood pressure, and
3 diseases for which there are not necessarily any
4 symptoms and which are chronic conditions for which
5 therapy will likely have to continue for a very long
6 time.

7 There is no way of titrating the dose of
8 the drug without repeat tests and evaluation of
9 results. Medical check-ups are needed periodically
10 for determining if the drug is working and for
11 assessing other aspects of the disease progression or
12 the evolution of adverse reactions.

13 For these reasons, we strongly oppose the
14 switching of these drugs from prescription to over-
15 the-counter status.

16 MODERATOR DeLAP: Thank you, Dr. Wolfe.

17 Do we have questions? Dr. Temple?

18 DR. TEMPLE: Actually, so let me ask you
19 the same question. It's been observed that a large
20 fraction of people with hypertension are not treated
21 by the current system, however it is, and the similar
22 phenomenon exists for people with treatable lipid
23 abnormalities, not people who shouldn't be treated.

24 Do you have any sympathy for the idea that
25 OTC availability would change that in a favorable way?

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1 DR. WOLFE: Well, two answers to that.
2 First of all, there is little question that our
3 colleagues in medicine have not done as good a job as
4 they should in detecting a lot of these diseases and,
5 when appropriate, treating them and should not be left
6 off the hook. And I think much more needs to be done
7 along those lines.

8 On the other hand, it is likely that the
9 benefit/risk ratio for people who are recruited
10 through the massive advertising that you correctly
11 project if these things are switched is going to be
12 much different and not as favorable as for -- not
13 always, but in a number of instances, there are people
14 who are going to get recruited with some of these low
15 borderline values that are going to be getting a risk
16 without any proven benefit. Namely, the proven
17 benefit of treating very low levels of cholesterol or
18 whatever else is just not there.

19 So I think that to essentially put a
20 larger number of people at risk and deprive them, in
21 a way, of evaluation because many of them are going to
22 be doing this on themselves, I think, is a big public
23 step -- public health step backwards. I think this is
24 a wake-up call to really remedy the situation within
25 the confines of the health care system as opposed to

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1 just making more things.

2 I mean, I would have some of the same
3 answers to the dangerous proliferation of herbal and
4 dietary supplements which are being used to treat some
5 of these same conditions. I mean, we essentially have
6 a lot of people out there who have or may have chronic
7 medical conditions, and I think it is no more sensible
8 to switch drugs that really need a proper medical
9 context from prescription to over-the-counter than it
10 is to have to labor, as we all do, under the confines
11 of this regressive 1994 law that puts all sorts of
12 other things on the market for people who didn't have
13 a chance to go to their doctor. I think they are both
14 dangerous kinds of moves.

15 MODERATOR DeLAP: Dr. Murphy?

16 DR. MURPHY: Dr. Wolfe, since no one wants
17 to put FDA in charge of reforming the health care
18 system, and we have heard that --

19 DR. WOLFE: I am in that group.

20 DR. MURPHY: I know. -- and we understand
21 that that may be part of some of the concerns here, in
22 your discussion would it make any difference if there
23 was a third process, as was discussed this morning,
24 both pros and cons, of the pharmacist interaction
25 after some initial requirement of a physician visit?

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1 DR. WOLFE: I have spoken a number of
2 times about the so called third class of drugs. This
3 country is in the minority, the distinct minority, as
4 opposed to majority in terms of not having this kind
5 of availability. This is an extra intervention of a
6 learned intermediary, pharmacists in this case.

7 I think that that might help for some of
8 these switches. I'm not sure that, for the issue of
9 hypertension or diabetes or cholesterol, that would be
10 appropriate. But certainly as a third alternative
11 between prescription and over-the-counter status for
12 some kinds of drugs, I think that might make sense.

13 It certainly worked out well in a number
14 of countries where it's been tried. I attended
15 probably six years ago, seven years ago, an
16 international meeting in Washington where
17 representatives from a number of countries that had
18 already used the third class of drugs talked about how
19 effective it had been and so forth.

20 So I think the idea is good. I think,
21 again, on a case by case basis it might be applicable
22 to some of these classes of drugs. It might not be to
23 others.

24 MODERATOR DeLAP: Dr. Jenkins?

25 DR. JENKINS: One of the questions we

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1 asked for feedback for in the Federal Register notice
2 was about what role the agency should take in
3 initiating switches in situations where the sponsors
4 have not initiated such a switch.

5 Can you give some thoughts about how you
6 would feel about that in the context of diseases or
7 classes of drugs that are already recognized as over-
8 the-counter appropriate drugs -- for example,
9 treatment of allergies, antihistamines, decongestants,
10 etcetera? What would be your thoughts?

11 DR. WOLFE: Well, the image of the
12 pharmaceutical industry kicking and screaming to
13 prevent a drug from being switched from prescription
14 to over-the-counter status is an amusing image,
15 because one of the cases that's been presented is one
16 where the company doesn't want it switched, but the
17 insurer -- the insurance industry does, because it
18 will relieve them of having to pay bills for
19 prescription drugs and dump the cost onto patients.

20 So the motivation is important. I think,
21 though, in the context of over-the-counter switches by
22 antihistamines, there was a time when serious
23 consideration was being given to switching terfenadine
24 or Seldane to over-the-counter, same with Hismanol,
25 and I think that the principle of waiting a

1 significant amount of time -- I would argue ten years
2 after a drug has been on the market -- so that the
3 chance of surprises is lower as opposed to higher,
4 would be important.

5 I mean, I remember -- this is probably 30
6 years ago, whatever -- when chlorfeneuramine maleate,
7 a drug I used to use and still use to treat people
8 with allergies because you can use a much, much lower
9 dose, get rid of the sedation for at least a number of
10 people. Physicians these days don't bother doing
11 that, because they've got all these other "non-
12 sedating" drugs around.

13 I think that the idea of waiting long
14 enough so that you are relatively sure that there's
15 not going to be any problem and then doing it does
16 make some sense. I mean, in other respects --
17 allergy, because it is capable of self-diagnosis -- it
18 is relatively short treatment for at least a lot of
19 people. There aren't a lot of people who are taking
20 these drugs around the year.

21 So I think that makes sense. I don't know
22 legally what one can do with a drug that is still on
23 patent to force a company to make an over-the-counter
24 switch. They have legal liability and things like
25 that. I think it's an interesting issue to look into.

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1 MODERATOR DeLAP: Other questions for Dr.
2 Wolfe? If not, thank you very much.

3 We'll move on to PEGUS Research, Dr. David
4 Bradford.

5 DR. BRADFORD: Good afternoon. The
6 colleague stumbling for the on/off switch here is the
7 President of our esteemed company, Dave McCammon. I
8 might mention that, contrary to what you may think,
9 the main goal of PEGUS Research is not the hiring of
10 researchers named Dave.

11 More germane to the point of the
12 discussion today, PEGUS Research is a pharmaco-
13 epidemiology research group that's been involved in a
14 number of OTC switch studies. My purpose here today
15 will be to discuss some of the design considerations
16 that we take into account in those trials in
17 suggesting some alterations in the strategy that the
18 FDA uses for considering the suitability of a drug for
19 an OTC switch.

20 Let me start by making my key point, which
21 is that it is my belief that the interests of public
22 health are better served by at least supplementing, if
23 not, more ambitiously, supplanting entirely the time
24 and extent of use criterion for assessing safety with
25 data from appropriately designed active safety trials.

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1 Let me start by making a few assumptions
2 explicit, at least for today's discussion. For this
3 discussion, which assumes that the key question in an
4 OTC switch is safety, I will assume that, first of
5 all, standard comparative trials have already
6 demonstrated efficacy for the switch candidate in the
7 proposed OTC dose for the proposed OTC indications;
8 secondly, that the safety of the drug in prescription
9 use has already been well characterized.

10 This is actually not a necessary
11 assumption, but for simplification of today's
12 discussion, I propose that as a second assumption.

13 Finally, that the basic question in an OTC
14 switch that must be answered is the question of
15 whether removing physician involvement in the drug use
16 process, which involves diagnosis in some form,
17 prescription of the drug, and monitoring drug use and
18 outcome, results in an unacceptable increase in public
19 health risk.

20 Implicit in this question is the issue of
21 comparative risk of OTC use versus prescription use.
22 If indeed the issue of comparative risk is fundamental
23 to the switch decision, a method for determining risk
24 under OTC conditions is required. However, the time
25 and extent of use criterion that has traditionally

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1 been employed relies heavily on various kinds of
2 passive surveillance such as MedWatch and reports in
3 the medical literature which are not particularly
4 useful nor ever really intended for estimating risk.

5 Here are some of the main reasons why.
6 First of all, the numerator in this proposed risk
7 estimate using passive surveillance sources is
8 significantly flawed. There are almost certainly
9 biases in the data of unknown extent and type
10 resulting from the fact that it is voluntary reporting
11 and that the voluntary reporting comes from a wide
12 variety of sources, and there is almost certainly
13 considerable underreporting, although the degree of
14 underreporting is, of course, not well known.

15 Therefore, the data which form these rate
16 estimates, the numerator for a rate estimate, are
17 inadequate. So we have a bad numerator. We have an
18 almost nonexistent denominator as point number two.

19 The most usual substitute for a use
20 denominator is sales figures, but there is essentially
21 no information available about the amount or
22 conditions of use for the persons for whom an adverse
23 event is reported.

24 Thirdly, the amount of information is
25 quite severely restricted in these passive

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1 surveillance systems, and there is almost no capacity
2 to query the data to find out more about the
3 relationship between the use of the drug and the
4 reported adverse drug event.

5 Finally, the data that are collected in
6 these systems are cases of prescription rather than
7 OTC use and, given the very substantial difference in
8 the nature of the usage patterns between prescription
9 and OTC use, that difference turns out to be a
10 potentially very significant one.

11 So in summary of this section then, while
12 passive surveillance is a cost effective means of
13 detecting the possibility of very rare adverse events,
14 its epidemiologic shortcomings are of such a
15 fundamental nature that simply accumulating more data
16 in the system fails to increase the value of the
17 information for assessing either adverse event rates
18 or the nature of the causal connection between drug
19 use and the adverse event.

20 Where passive surveillance then fails,
21 active surveillance can succeed very well, provided it
22 is designed correctly. I will next sketch the
23 research design principles which I believe will
24 produce the best data to answer the switch question
25 that I outlined earlier.

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1 The overarching principle is that subjects
2 should be evaluated in a setting that's as similar to
3 the actual conditions of OTC use as possible. Points
4 2 through 8 really are just elaborations,
5 particularizations of this broad general principle.

6 First of all, subjects should self-select
7 into the trial, and if the trial is designed to have
8 an active comparator, subjects should be allowed to
9 self-select into the treatment arm of their own
10 choice.

11 Thirdly, it should be an all-comer study.
12 That is, all subjects who self-select into the trial
13 should be allowed to participate.

14 Next, the study must be an open-label
15 study to reflect the patterns of use and selection and
16 decisions about use that take place when a consumer
17 makes the decision to use an OTC drug.

18 Assessment of drug use and outcome, which
19 is not -- should be unobtrusive. This is not a
20 particularly big problem in standard randomized
21 blinded trials, but in these kinds of trials it's
22 important that the measurement of the process doesn't
23 influence the process itself.

24 The sixth point is that the studies should
25 be relatively large. We propose that they should be

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1 able to detect roughly one order of magnitude more
2 sensitively the occurrence of rare adverse events, and
3 we suggest somewhere on the order of one in a thousand
4 to three in 10,000.

5 Point number seven is that subject
6 recruitment and enrollment procedures should be as
7 simple and realistic as possible to produce a sample
8 that is truly representative of OTC subjects.

9 Finally, recruitment and enrollment should
10 be done in sites where people go to obtain their OTC
11 medications, a point which has been raised in earlier
12 discussions today.

13 Let me just add a note in passing about
14 randomized blinded trials. These studies, of course,
15 are the sine qua non of efficacy evaluation. We don't
16 have anything better nor is there anything better
17 likely to emerge. However, they are the wrong tool
18 for assessing safety in actual use, especially OTC
19 use, as they impose constraints on the subject sample
20 and conditions of use which are entirely
21 uncharacteristic of the self-selection and use
22 patterns consumers engage in who seek OTC treatment.

23 In summary then, let me conclude with
24 these points. Properly designed safety trials can
25 provide important information which is directly

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1 relevant to this fundamental question of drug safety
2 in OTC use.

3 Active surveillance studies can provide
4 true adverse event rate estimates relatively quickly.
5 Therefore, decisions about a potential switch can be
6 made much more quickly and efficiently and with
7 greater accuracy.

8 Finally, active surveillance may be
9 particularly useful for drugs that have a relatively
10 low prescription use rate where it would require a
11 large amount of time for data to accumulate in a
12 passive surveillance systems for those that are being
13 proposed for a direct-to-OTC sale and for those that
14 are on a fast track for OTC approval.

15 So in conclusion, I believe that OTC
16 switches based on properly designed, active
17 surveillance studies will provide better switch
18 decisions in a more timely fashion than can be done
19 using the data from passive surveillance.

20 That concludes my presentation. Thank
21 you.

22 MODERATOR DeLAP: Dr. Woodcock?

23 DR. WOODCOCK: I just want to make sure I
24 understand your ideas. The study design you outlined,
25 it seemed, would be useful for determining if

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1 inappropriate people self-select, if people are
2 incapable of diagnosing their condition, if people are
3 failing to seek medical care for deterioration of
4 their self-diagnosed condition.

5 Are those the type of adverse events you
6 are talking about? Are you actually talking about the
7 known kind of adverse events?

8 DR. BRADFORD: Actually, both of those are
9 very easily handled in this kind of design. Data are
10 collected about the nature of the enrollment
11 population, including those who are presented with a
12 decision about enrollment and then choose not to
13 participate in the trial. That is, to not use the
14 drug. But these trials also include specific methods
15 of following up on use and outcome in order to find
16 out what the consequences of use were and to correlate
17 that with the way the drug was used.

18 DR. WOODCOCK: Are you contemplating
19 there's something -- Is that what you're calling
20 active surveillance or are you calling active
21 surveillance a wide variety of things of which that
22 was an example?

23 DR. BRADFORD: I'm just contrasting active
24 surveillance with the sort of passive surveillance
25 that comes as a consequence of data accumulating in a

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1 spontaneous reporting system.

2 DR. WOODCOCK: Okay. Thanks.

3 MODERATOR DeLAP: Dr. Temple?

4 DR. TEMPLE: It would actually be helpful
5 if you could indicate without giving anything away an
6 example of where you would use this and what kinds of
7 things you would be looking for.

8 I ask that, because my worry would be that
9 in selecting one of a class of drugs, people might
10 select differently, depending on their past history,
11 and you might be misled. Just for example, if you
12 wanted to compare a sedating and a non-sedating
13 antihistamine, people who have trouble with sedation
14 probably would choose one, and people who didn't might
15 choose the other, and they might be fundamentally
16 different with respect to their likelihood of having
17 car wrecks and stuff like that -- you know, all the
18 problems that come up when you don't randomize.

19 So the other reason I ask is that even a
20 good sized study of 20,000 would be detecting sort of
21 relatively common risks, not the sort of odd, bad
22 torsade de pointe or something like that.

23 So when -- Can you say a little more
24 precisely when you might use this?

25 DR. BRADFORD: Sure. The usual

1 constraints that are -- The cost constraints that are
2 associated with studies of this type would probably
3 limit them to 20,000 or less, although certainly there
4 are instances of studies that go up into the 40-80,000
5 range. Those indeed will detect probably at best
6 something on the order of one in 10,000, which is a
7 pretty reasonable goal for a study like this to
8 accomplish.

9 If I understand the other part of your
10 question, it has to do with the nature of the actual
11 process of evaluation itself. I think it would not
12 inappropriate to mention our experience in the
13 assessment in the safety of Denavir, which was
14 considered by the Advisory Committee some months ago.

15 One of the interesting things about that
16 trial was that, although the demographic profile of
17 subjects was quite different from the population
18 demographics, it matched almost identically the
19 information that was obtained about cold sore
20 sufferers themselves.

21 So we were able, on the basis of the
22 enrollment criteria that we used, to gather a sample
23 that looked like it was very representative of the
24 potential target population.

25 Now with respect to the question of

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1 sedating versus non-sedating antihistamines, one of
2 the crucial elements of that is how do people self-
3 select? So one of the possibilities in a trial of
4 this kind where you allow people to self-select and
5 the conditions is determining what it is that -- how
6 those populations differ from each other, what the
7 characteristics of each population is.

8 DR. TEMPLE: Okay. I'm still a little --
9 I understand you're sort of making sure everybody
10 reports actively, so you get a complete enumeration of
11 everything that happened to them. I guess that's more
12 important than the comparative aspect of it.

13 DR. BRADFORD: Yes. The safety
14 assessment, we would argue, is fundamentally a
15 noncomparative kind of activity.

16 MODERATOR DeLAP: Dr. Jenkins.

17 DR. JENKINS: This is a very interesting
18 study design that you proposed. As you know, the
19 devil is always in the details. I was interested in
20 your item number 3 where you say that all subjects who
21 self-select into the trial should be allowed to
22 participate.

23 Can you comment on how you would actually
24 deal with someone who self-selects who is clearly,
25 obviously contraindicated for use of the drug, say a

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1 woman who is obviously pregnant self-selects to use
2 the drug even though the drug label says not to use if
3 you are pregnant. Would you still enroll that patient
4 into the study, and how do you deal with the ethics of
5 that?

6 DR. BRADFORD: Yes. Our argument is that
7 any drug that is being proposed for a true OTC switch
8 -- that is, an OTC switch in the environment that we
9 operate in here in the U.S. -- for whom there is no
10 learned intermediary to, in fact, intervene needs to
11 be allowed into the trial, because under OTC
12 conditions that person would be able to purchase the
13 project, even in spite of recommendations against its
14 purchase.

15 So one of the issues that's important to
16 understand is, when they self-select into the trial,
17 do they in fact actually use the drug. Under what
18 circumstances do they use it, and what is the outcome
19 of use for those subjects who would be free to use it
20 if, in fact, it were approved for OTC sale.

21 Now there may be some intermediate studies
22 that need to be done if the safety of the drug is
23 still in question, but for most of these drugs the
24 safety issues have been reasonably well resolved, at
25 least to the point of being able to make the case for

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1 an OTC switch.

2 DR. JENKINS: Can you clarify if what you
3 just described is a hypothetical or have you actually
4 applied that to a study situation? I'm just thinking
5 that most people would have ethical concerns with that
6 type of study design, and I'm thinking that most
7 sponsors would have serious liability concerns about
8 enrolling patients into such trials.

9 DR. BRADFORD: Well, it is important to
10 make sure that these are adequately reviewed by ethics
11 committees and also approved by the FDA. But it seems
12 to me that the FDA is in much better decision to make
13 a decision about the suitability of a switch if they
14 have that kind of information available to them.

15 So rather than taking a drug to market for
16 which there is no data of that sort available at all,
17 it seems like a very sensible thing for the agency to
18 require that kind of information.

19 DR. JENKINS: Do you have experience
20 actually applying this model in a successful trial?

21 DR. BRADFORD: We have had the experience
22 in two of about six trials. In the other instances,
23 some of these considerations have prevented the
24 sponsor from wanting to continue in that regard.

25 We would encourage the FDA to consider the

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1 need to have that kind of information, though,
2 available.

3 MODERATOR DeLAP: Well, it's been a
4 conundrum, I think, for the agency over the years.
5 How do you know about things like safety of use in
6 pregnancy, which you know happens for these products
7 that are in the OTC marketplace. How do you know
8 that, if you don't study it, and yet how do you study
9 it?

10 So it's a real puzzle, and I'm always
11 interested in different views on the subject.

12 If there are no other questions, we'll
13 continue. Thank you very much. Next we have Amy
14 Alhna for the National Women's Health Network.

15 MS. ALHNA: Thank you. I'm speaking today
16 on behalf of the National Women's Health Network,
17 which is a nonprofit women's health advocacy
18 organization. We are supported by more than 10,000
19 individual and 300 organizational members, and we
20 accept no financial support from pharmaceutical
21 companies or medical device manufacturers.

22 In the 25 years since the Network was
23 founded, we have spoken at a number of FDA meetings
24 that have been called to consider whether specific
25 drugs should be made available over-the-counter, and

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1 sometimes we've supported the shift, and sometimes we
2 have opposed it.

3 Just as we know the agency is striving for
4 a consistent set of standards to use in making these
5 determinations, we have also tried to be consistent in
6 the positions that we have taken.

7 My comments today will address a number of
8 specific types of products, as well as some of the
9 more general issues relating to consumer understanding
10 and to the structure of the regulatory system. I'm
11 going to start with talking about the specific
12 products.

13 The Network is strongly committed to the
14 development of topical microbicides which women will
15 be able to use to protect themselves against STD and
16 HIV infection. We believe that, in order for
17 microbicide products to be used widely and
18 effectively, there will have to be some that are
19 available without prescription.

20 There's currently a range of products in
21 development, some of which are likely to be
22 appropriate for over-the-counter distribution, and
23 others may need to start as prescription products.
24 While the safety standard for OTC distribution should
25 not vary from product to product, some microbicides

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1 will be able to meet that standard more easily and/or
2 more quickly than others.

3 Those products which have already been
4 approved for other uses and, therefore, have an
5 established safety record are likely to be able to
6 demonstrate sufficient safety for OTC distribution
7 more easily than products which are entirely new.

8 Based on our understanding of the
9 microbicides in development, we are suggesting that
10 the FDA might consider these products in four tiers:
11 First, products with an established safety record in
12 vaginal or rectal use, which is the area where they
13 will be used; second, products with an established
14 safety record in contact with other mucosal tissue;
15 and third, products with an established safety record
16 in topical use on non-mucosal tissue; finally, new
17 chemical entities that don't have an established
18 safety record.

19 I know that you will hear more about each
20 of the products that I'm going to talk about tomorrow.
21 So I'm going to keep my comments brief.

22 The second product I want to talk about is
23 oral contraceptive pills. While the Network would
24 like to see more OTC contraceptive options made
25 available to women, we oppose the OTC distribution of

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1 oral contraceptive pills for continuing, regular
2 contraception.

3 We believe that prescription status for
4 regular oral contraceptives is necessary to maintain
5 effective use of this method and to protect the health
6 of women who choose to use it. Experience in Sweden
7 and other countries has demonstrated that when the
8 pill is distributed with no counseling and no
9 opportunity for dialogue about the method, effective
10 use declines.

11 In addition, we have concerns about the
12 health impact of OTC distribution of the pill without
13 a prescription requirement. There will be no
14 opportunity for a health care provider to screen out
15 users who should not be taking the pill over the long
16 term, and the opportunity for preventive health care
17 and disease detection will be lost, which is a
18 particular concern when it comes to women of color and
19 to low income women who are already likely to have
20 decreased access to such health services.

21 If a third alternative between the current
22 prescription status and OTC distribution were
23 available in the United States such as distribution by
24 pharmacists from behind the counter, the Network would
25 support distribution of oral contraceptives in that

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1 way. In the interest of time, I should just say here
2 that we support the establishment of such an
3 alternative.

4 The final product I want to talk about is
5 emergency contraceptive pills, "morning after" pills.
6 It's already been mentioned a couple of times today.
7 The Network believes that the medical and economic
8 issues raised by emergency contraceptive pills are
9 different from those associated with the ongoing use
10 of oral contraceptives.

11 Recognizing that there are communities
12 where even pharmacist distribution will not resolve
13 the barriers that currently prevent women from having
14 timely access to the method, the Network would support
15 over-the-counter distribution of emergency
16 contraceptive pills under the following conditions.

17 We believe there must be appropriate label
18 warnings to protect the health of women with
19 contraindications to the use of emergency
20 contraceptive pills. We would like to see there
21 continuing to be a prescription option to ensure that
22 OTC availability doesn't raise new barriers to access
23 for those women who do have insurance coverage of
24 prescription contraceptive options, and finally that,
25 as with any other OTC product, women have to have

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1 access to clear, complete and accurate information
2 about the product.

3 Package inserts for emergency
4 contraception products should be available in multiple
5 languages, should employ techniques for women who
6 cannot read such as using pictorial representations as
7 appropriate.

8 Now I'm going to move on to talking about
9 consumer understanding. One of the underlying
10 principles that guides the Network's work is that
11 informed consumers can make good health care decisions
12 for themselves. The definition of an informed
13 consumer, however, is critically important to the
14 realization of this principle.

15 We need to trust people with complete
16 information rather than withholding details that
17 commercial sponsors or health care professionals may
18 fear will complicate or bias the consumer's decision.

19 The FDA needs to ensure that consumers
20 have access to unbiased information about the products
21 that the agency regulates. Here, I think it's
22 especially important to say that advertisements paid
23 for by commercial sponsors which are designed to sell
24 a product are not adequate information sources for
25 consumers.

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1 The need to ensure consumer access to
2 unbiased and complete information is greatest where
3 the advertising campaigns are the most intense and the
4 budgets highest. That is in the area of OTC drug
5 products, although direct consumer advertising of
6 prescription products is certainly making a run for
7 it.

8 The only source of information that the
9 vast majority of consumers have about a drug other
10 than an advertisement is the information that's
11 included on or in the product package. The
12 information on the product label and in the patient
13 package inserts must be carefully reviewed and
14 assessed by the FDA to determine that it's complete,
15 accurate, and easily understood by potential users of
16 the product.

17 The Network supports the use of a
18 standardized label format for OTC products with
19 consistent categories and placement to make it easier
20 for consumers to find the important information on a
21 product label, and to make it possible for consumers
22 to learn how to find the information they need easily.

23 One of the specific questions the FDA
24 raised in this context of consumer understanding in
25 the notice for the hearing is whether a prevention

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1 claim can encourage ill advised behavior.

2 Taken in the context of microbicides, for
3 example, we understand the agency to be asking whether
4 the availability of products that claim to prevent or
5 reduce the risk of transmission of sexually
6 transmitted disease will lead to an increased
7 willingness on the part of consumers to risk exposure
8 to disease.

9 The Network feels strongly that a product
10 which offers partial protection and does not entirely
11 eliminate risk can be used safely, as long as clear
12 information about risk and protection is conveyed to
13 the consumer. In fact, in the field of contraception
14 there are research models which demonstrate that a
15 less efficacious product used more consistently can
16 actually increase the level of infective protection.

17 Products which are easier to use
18 consistently than condoms, such as microbicides,
19 therefore, may actually be more effective in
20 preventing the spread of STDs, even if they have a
21 lower theoretical efficacy rate than condoms.

22 Furthermore, we believe that this question
23 reflects a tendency in this country to equate morality
24 with health. We believe the association is
25 inappropriate and unfounded. There is no

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1 scientifically valid evidence that prevention claims
2 lead to increased risky behavior, much less to an
3 increased incidence of disease.

4 The Network feels strongly that, if clear
5 information can be conveyed to consumers regarding a
6 product which offers partial protection and does not
7 entirely eliminate risk, then consumers can make
8 responsible and informed decisions about their
9 behavior based on that information.

10 Thank you again for the opportunity to
11 speak today and to provide you with our comments.
12 I'll take questions, if there are any.

13 MODERATOR DeLAP: Thank you. Well, it
14 looks like you did a very good job of covering all the
15 bases.

16 MS. ALHNA: Thanks.

17 MODERATOR DeLAP: Thank you. Our next
18 speaker will be representing the Pharmaceutical
19 Research and Manufacturers of America, Russell
20 Bantham, Deputy General Counsel.

21 MR. BANTHAM: Thank you, Dr. DeLap. My
22 name is Russ Bantham. I'm General Counsel for the
23 Pharmaceutical Research and Manufacturers of America.
24 PhRMA represents the country's leading research based
25 pharmaceutical and biotechnology companies which are

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1 devoted to inventing medicines that allow patients to
2 lead longer, healthier and more productive lives.

3 Our members this year will invest over \$26
4 billion in research and development. With the
5 announcement earlier this week regarding the human
6 genome project, that \$26 billion investment is even
7 more important.

8 Prescription drugs discovered and
9 developed by PhRMA members are the source of virtually
10 all major new OTC products today. PhRMA, therefore,
11 has a vital interest in the subjects being considered
12 by FDA today at this hearing. I will focus my
13 testimony on the matters of greatest interest to PhRMA
14 and will file more detailed post-hearing comments in
15 accordance with the notice.

16 The principal issues that I want to
17 address today concern the role of the sponsor in
18 initiating an Rx to OTC switch and the criteria to be
19 applied by FDA in reviewing switch applications.

20 The questions presented in the hearing
21 notice suggest that FDA is considering whether it may
22 decide to switch a drug from prescription to
23 nonprescription status without the participation or
24 even over the objection of the holder of the approved
25 NDA for the drug for prescription use.

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1 In our view, this would be both unlawful
2 and contrary to the goal of protecting public health.
3 Under our regulatory system FDA reviews applications
4 submitted by sponsors for uses they have presented in
5 their proposed labeling. It's not within the FDA's
6 authority to force a manufacturer fundamentally to
7 change the conditions of use of its product from
8 prescription to nonprescription status.

9 The switch of a drug would alter the terms
10 of an approved NDA for a prescription drug by removing
11 the Rx legend and changing the labeling from a
12 physician package insert to consumer oriented
13 directions. Under Section 505(e) of the Food, Drug
14 and Cosmetic Act, FDA cannot make such changes over
15 the objection of the sponsor without following the
16 notice and hearing process that protects the rights of
17 the NDA holder.

18 FDA cannot use rulemaking to circumvent
19 this process. There is a procedure in 503(b) of the
20 Act which has been referenced earlier dating back to
21 1951 for the issuance of so called switch regulations,
22 but as also was mentioned, this process hasn't been
23 used since 1971 before the institution of the OTC drug
24 review and before the Hatch-Waxman amendments in 1984.

25 The switch regulation procedure was never

1 used, and certainly can't be used over the objection
2 of a sponsor, to avoid the sponsor's hearing rights
3 under 505(e). As a matter of both administrative law
4 and procedural due process, FDA could not switch a
5 drug through informal rulemaking without the consent
6 of the holder of the approved NDA that would be
7 changed through the switch.

8 Forced switches would also violate a
9 sponsor's proprietary rights and their own safety and
10 efficacy data. Any switch will be based in
11 substantial part on the demonstrated safety and
12 effectiveness of the underlying prescription drug.

13 The full reports of studies that provide
14 proof of safety and substantial evidence of
15 effectiveness reside in the sponsor's NDA. They
16 cannot be relied on by the agency to support
17 regulations or approvals that would allow anyone else
18 to manufacture and sell the drug for either
19 prescription or nonprescription use except to the
20 limited extent provided by the Hatch-Waxman
21 amendments.

22 The current system under which switches
23 are initiated by NDA sponsors through the submission
24 of new applications or supplements serves the public
25 health well. Extensive prescription use, as Dr. Wolfe

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1 noted, is an essential part of the full
2 characterization of a drug's clinical profile.

3 Moreover, manufacturers have the most
4 comprehensive and detailed knowledge of their drugs,
5 including information bearing on whether a drug is a
6 suitable switch candidate. Taking all of this
7 information into account, manufacturers are in the
8 best position to decide when to begin the switch
9 process and thereby avoid premature switches that
10 could put some members of the public at risk.

11 In addition to poorly serving consumers,
12 a forced switch approach would unfairly force
13 manufacturers to bear product liability risks
14 associated with OTC use, even if they believe that a
15 drug should remain available only by prescription.

16 The manufacturers are also in the best
17 position to invest in developing the additional data
18 needed to support a switch. Any switch today requires
19 extensive data in addition to what's in the NDA for
20 prescription use.

21 Switches proposed on the basis of
22 conclusory assertions by third parties that are not
23 privy to all of the data on the drug and who are
24 unwilling or unable to fund the necessary studies to
25 support the switch should be summarily rejected.

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1 Several of the questions in the hearing
2 notice concern the criteria to be used by FDA in
3 evaluating applications to switch drugs from
4 prescription to nonprescription status. We believe
5 that FDA should apply the same approach to these
6 applications that it does to any other NDA. That is
7 to evaluate each switch application on the individual
8 merits based on the statutory criteria of safety,
9 effectiveness and proper labeling.

10 Thus, for example, nothing in the Act
11 authorizes FDA to declare an indication or a disease
12 state to be exclusively prescription or
13 nonprescription. The question must be addressed in
14 the context of each drug intended to treat or prevent
15 the disease based on its particular risk/benefit
16 profile and labeling.

17 There is nothing at all incongruous about
18 the simultaneous availability of both prescription and
19 nonprescription drugs for the same conditions. This
20 is true today across a wide variety of disease states.
21 Moreover, it promotes sound public health policy by
22 providing consumers the options of both self-
23 treatment, where that is appropriate, and consultation
24 with a physician and treatment with a prescription
25 drug, where that is appropriate.

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1 It wouldn't make sense to declare a
2 disease off limits to prescription drug therapy and
3 thereby discourage both consumers from consulting with
4 their physicians and manufacturers from investing in
5 the development of new products.

6 As another example, any suggestion that
7 FDA take into account the relative economics of
8 prescription and nonprescription distribution must be
9 rejected. FDA's relevant statutory authority relates
10 exclusively to drug safety, effectiveness and
11 labeling. The agency has no authority to consider
12 prices or related matters as part of the approval
13 process.

14 FDA certainly should not allow its agenda
15 to be dictated by insurers that are motivated to
16 request switches in order to shift costs from their
17 own prescription drug benefit programs onto consumers.
18 Any change in policy to allow FDA or third parties to
19 initiate switches would unnecessarily encumber the
20 drug development process, chilling many areas of
21 research and development and complicating the already
22 difficult considerations that underlie the decision to
23 proceed with drug development.

24 In conclusion, we commend FDA for holding
25 this hearing on this important subject of Rx to OTC

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1 switches and other aspects of nonprescription drug
2 regulation. FDA should retain its existing policy of
3 making switch decisions through the evaluation of NDAs
4 and supplements filed by manufacturers, based on an
5 individual assessment of the safety and effectiveness
6 data and proposed labeling for each specific switch
7 candidate.

8 This is the approach -- This approach is
9 the one that FDA must follow in accordance with the
10 law. It also protects and ensures the safety of
11 consumers.

12 Consumers should have the widest possible
13 array of treatment options, both prescription and OTC,
14 in an environment that is conducive to investment in
15 drug research and development, because only through
16 continued research and development will consumers have
17 more treatment options, both prescription and OTC, in
18 the future. Thank you very much.

19 MODERATOR DeLAP: Thank you. Dr.
20 Woodcock.

21 DR. WOODCOCK: Yes. I would like to
22 comment and then ask you a question, because I've
23 heard a recurring theme that people feel we are asking
24 should we be making relative -- comparative, I guess,
25 decisions, and it's been pointed out numerous times

1 during the course of today, we don't have the
2 authority to do that.

3 I would like to point out that the concept
4 of safety -- It has also been pointed out that,
5 really, no pharmaceutical is absolutely safe. There
6 is no absolute safety of an active drug. Therefore,
7 concept of safety for a drug is really a contextual
8 one. It depends on the context.

9 For example, products that were considered
10 safe in 1900 would be considered, many of them, to
11 have terrible side effects and be unacceptable as
12 treatments today in the year 2000. Therefore, the
13 concept of safety has some contextual quality to it,
14 and it can't be -- It's not a stand-alone assessment,
15 in my opinion. I'd like you to comment on that.

16 MR. BANTHAM: I agree with that, but I
17 think that's FDA's most important job, to do that
18 balancing of risk and benefit.

19 DR. WOODCOCK: Okay. But part of that
20 context then for any pharmaceutical does have to do
21 with the available armamentarium, not just drugs but
22 other treatments. Therefore, arsenic which used to be
23 used for certain treatments really wouldn't be
24 acceptable nowadays. You see what I mean?

25 MR. BANTHAM: I do.

1 DR. WOODCOCK: Okay. Just so that's clear
2 to everyone, we are not really saying, oh, you're
3 going to compare all these drugs, you know, their
4 effectiveness, to one another and so forth and so on.
5 There is a context in which drugs are made available,
6 and we all hope through research and development that,
7 as time progresses, the armamentarium will become
8 overall safer for everyone.

9 MR. BANTHAM: That's correct.

10 MODERATOR DeLAP: The thing I like to say
11 is that we like consumers to have choices about drugs,
12 but we want to make sure those are good choices.
13 There is no point in having a drug out there if it's
14 outlived its usefulness.

15 For example -- I'm not speaking in the
16 context of any particular drug or class right now, but
17 as the years go by and as we get better drugs that do
18 a little better job and effectiveness and may be
19 safer, there may be times that come when there is a
20 drug that's outlived its usefulness, and we'll have to
21 say there is no good reason that a consumer should
22 choose this drug. So why do we offer it as a choice
23 in the marketplace?

24 Dr. Temple?

25 DR. TEMPLE: I think someone answered that

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1 before. If a drug has outlived its usefulness and is
2 too toxic, whether it's Rx or OTC, we would follow the
3 usual procedures and get rid of it.

4 I guess I want to probe a little further
5 the idea that we should have little to no role in
6 suggesting that certain drugs might be usefully
7 available over-the-counter.

8 Dr. Wolfe suggested it takes ten years.
9 That would be one answer. I think we thought three or
10 four is usually enough, and I guess a usual answer we
11 get is about one year before the drug goes off patent.

12 Now these are various ways of making that
13 decision, and apart from the question of what process
14 we would have to follow if we wanted to do that -- and
15 I guess I also want to note that I don't know anybody
16 who ever contemplated taking one of these making a
17 monograph drug. I think we were talking of -- In our
18 wildest dreams, we've been thinking of asking for a
19 supplement, you know.

20 How far do you want to push this? Don't
21 you think it's worth discussing whether something now
22 prescription might have an advantage or might also
23 need to be available, along with other drugs that are
24 available in the OTC market?

25 To say no seems to sort of fly in the face

1 of some of the arguments about why it would be so good
2 to have, say, lipid lowering drugs over-the-counter.
3 That's an argument about what should be widely
4 available so people can use it. You can make the same
5 argument in reverse for drugs that lack certain side
6 effects that other OTC drugs have.

7 How far are you pushing that or are you
8 just wanting to say the company should be involved; we
9 shouldn't be high-handed?

10 MR. BANTHAM: No, but I think the
11 difficult is answering the question in the abstract.
12 You can have an interesting philosophical discussion,
13 when is the appropriate time, and people have
14 different views, depending on their personal opinions
15 or wherever they are coming from in the health care
16 system.

17 I think that's why you have to take it
18 drug by drug and look at the weight of the evidence
19 and using FDA's traditional benefit/risk calculus,
20 they are in the best position to make that judgment.

21 The real question is who initiates the
22 process. It seems to me, you just can't have a
23 process that's totally open. The system that we have
24 is the system where the sponsor initiates the switch
25 process. That seems to us to be the best system.

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1 It's working.

2 There isn't a real reason to change that,
3 and there are a lot of good reasons why that system
4 that we have that's embodied in the law is one that
5 should continue.

6 There are, obviously, people who have
7 different points of view, and forums like this are
8 opportunities to get those points of view out. But
9 when you get down to making judgments, it's really
10 difficult to generalize. You really have to -- You
11 can't look category by category, because within
12 categories there are different drugs that have
13 different safety and effectiveness profiles.

14 The process allows for the petition to be
15 filed, the data supporting that, the labeling
16 supporting that. FDA then goes through the review
17 process and makes a judgment on behalf of the public,
18 and that system seems to be a very good one.

19 DR. TEMPLE: Well, I mean, from time to
20 time we've suggested to companies that it was time for
21 an efficacy supplement for something or other, because
22 we were aware of a cooperative group study or
23 something like that, and the company wasn't doing
24 anything.

25 In fact, we've sort of promised to do that

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1 in some settings when we were aware of uses that were
2 off-label and that seemed to have good support. Isn't
3 this sort of like that, that if we were aware of a
4 potential useful switch, would it be unreasonable to
5 ask the company if they were interested? I mean, you
6 don't object to that? You just don't want us to be
7 able to force it.

8 MR. BANTHAM: No, not at all. Through
9 discussion, companies may make decisions --

10 DR. TEMPLE: Come around.

11 MR. BANTHAM: -- based on the merits. I'm
12 sorry. I didn't hear your comment.

13 DR. TEMPLE: I said come around. That's
14 our informal way.

15 MR. BANTHAM: That happens, too.

16 MODERATOR DeLAP: Yes, Dave Fox.

17 MR. FOX: In your view, what's the status
18 of Section 503(b)(3) of the Act, the provision that
19 authorizes the agency by regulation to remove a
20 prescription restriction on a new drug if it's in the
21 public interest to do so, if it's consistent with
22 public health?

23 MR. BANTHAM: I think that's an
24 interpretation. I don't think the words actually say
25 that.

1 MR. FOX: The provision I'm referring to
2 is --

3 MR. BANTHAM: You mean the switch
4 provision?

5 MR. FOX: The switch regulation, yes.

6 MR. BANTHAM: Yes. It's not used. I
7 mean, it's there.

8 MR. FOX: But I was just going back to
9 your remarks. I'm trying to figure out whether you
10 think it's legally a dead letter somehow as a result
11 of the initiation of the OTC review and somehow as a
12 result of Hatch-Waxman, or do you think it's just
13 unused but legally viable?

14 MR. BANTHAM: It exists in the law, but
15 there's no procedure. There's no -- There's just
16 nothing there that I understand. I mean,
17 theoretically, something could be, I suppose, fit
18 within those words to make that an operative section,
19 but there isn't one now.

20 As someone said, it's an antique.

21 MR. FOX: Museum piece.

22 MR. BANTHAM: It's just not used.

23 MR. FOX: I'm just trying to understand.

24 MR. BANTHAM: It's clearly there and
25 provided for. It's just a mystery what --

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1 MR. FOX: And there are regulations that
2 implement it that still exist as well. So I mean,
3 there's a disconnect, I think, between that -- We have
4 this extra provision. We have the regulations as to
5 what more process or regulation we would need to carry
6 out what's contemplated under 503(b)(3).

7 MR. BANTHAM: I don't have an answer,
8 because I would be just speculating.

9 MODERATOR DeLAP: Charlie.

10 DR. GANLEY: Yes. I just want to go back
11 to two of your comments. One is that the agency has
12 no authority to consider prices or related matters as
13 part of the approval process. I think, generally, we
14 follow that.

15 The other concept, that manufacturers are
16 in the best position to decide when to begin the
17 switch process and thereby avoid premature switches
18 that could put some members of the public at risk.

19 I guess the question that, if the FDA is
20 looking at a particular product and views that it
21 would be in the public interest to have it in the OTC
22 market, why shouldn't we initiate some process to do
23 that?

24 I mean, we are going through various
25 phases here with accepting foreign ingredients in the

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1 future that have absolutely no marketing experience.
2 They have OTC marketing experience in other countries.
3 Yet we have products in this country that are marketed
4 Rx that are in OTC markets in other parts of the
5 world.

6 So why is it the company that is the only
7 one who is to make the cut here?

8 MR. BANTHAM: Well, I think, if FDA wants
9 to initiate that and the manufacturer or sponsor is
10 agreeable, I don't see any problem. I think we're
11 worried about the situation where there isn't
12 agreement, for reasons that I'm not sure, whether they
13 are based on safety, whether they are based on a
14 concern over whether OTC use is appropriate. There's
15 been enough time or enough experience with the
16 prescription use to satisfy the safety requirements,
17 and the sponsor did not agree with the suggestion.
18 Then there is a concern.

19 My comments really went to that.

20 MODERATOR DeLAP: I think the people that
21 write the laws made a lot of effort to try and have
22 the incentives match up with the public health goals
23 of regulations of drugs in this country. One can
24 always envision that at times, despite those efforts,
25 that the incentives may not exactly align with the

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1 public health interests.

2 I think what we are grappling with is how
3 we still can get those public health interests met.

4 Dr. Jenkins?

5 DR. JENKINS: I have a question. I wanted
6 to go back to your statement. You say in here that
7 FDA's relevant statutory authority relates exclusively
8 to drug safety, effectiveness and labeling. The
9 agency has no authority to consider prices or related
10 matters as part of the approval process.

11 I'm wondering, by that do you mean that
12 when we get an OTC switch presentation from the
13 sponsor that we are limited solely to considering the
14 drug's safety, effectiveness in the intended patient
15 population who would use the drug, that the drug would
16 be safe and effective in that population, and that we
17 have to exclude all consideration of population or
18 societal benefits of the switch?

19 For example, societal benefits may be that
20 there's an overall reduction in mortality if this drug
21 were made available over-the-counter. Are you saying
22 we can't consider that, and we have to limit our
23 consideration to the safety and effectiveness in the
24 actual patients who might use the drug, and not a
25 broader societal context?

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1 MR. BANTHAM: I think that's what the
2 statute provides, and I think Dr. Wolfe's comment
3 about who is responsible for reforming the health care
4 system -- that lies someplace else in our system.

5 DR. JENKINS: Thank you.

6 MODERATOR DeLAP: Okay. If there are no
7 further questions, thank you very much.

8 Our next speaker is Peter Barton Hutt, who
9 has played many roles over the years, but today is
10 representing himself.

11 MR. HUTT: Thank you, and good afternoon.
12 As Bob mentioned, I am appearing today not on behalf
13 of any client or group. I am here to represent my own
14 personal views.

15 It occurred to me when I read the Federal
16 Register notice that you were grappling today and
17 tomorrow with identical issues that those of us who
18 were in the agency 30 years ago grappled setting up
19 the over-the-counter drug review and, therefore, that
20 our experience and the lessons learned from that grand
21 effort might be useful in some of your deliberations.

22 I will again emphasize, these are my own
23 personal views, and no one else's.

24 Now I'd like to make four points. The
25 first one is that we discovered in the early 1970s

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1 that the absolute essential element of any successful
2 OTC drug program was a very visible, strong OTC
3 presence in the Food and Drug Administration.

4 When the OTC drug review was initially
5 started by FDA, it resided in the then-Bureau of
6 Drugs, now, of course, the Center. It was almost
7 immediately taken out of there and put in the
8 Commissioner's Office, because it became clear that it
9 would be drowned out by the entire rest of the Bureau
10 responsibilities and would not have an opportunity to
11 do the job that was needed.

12 That was an extraordinarily productive
13 first five years of the OTC drug review. It was then
14 put back down in the Bureau at a relatively low
15 position and, I will have to say, that was the
16 beginning of the slide downward in terms of its
17 productivity.

18 It was returned to Office status within
19 the Center, then the Center, in the early 1990s. I
20 believe it again began to develop a vibrant and very
21 cohesive OTC drug philosophy and program. Once again,
22 however, in the mid-1990s it was put back down lower
23 in the organizational structure, and I believe that
24 that is why today we have need for a hearing like this
25 in order to try to develop a more coherent and sound

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1 program for the future.

2 It is quite clear to me, based on watching
3 this for 30 years, that if there is any hope for a
4 truly sound, well thought through, and very public OTC
5 drug program in the Food and Drug Administration, it
6 is going to have to rely on a visible office, not a
7 division, staffed with people who are dedicated to
8 this area of product, who have the responsibility and
9 the resources to go with it. Certainly, that is what
10 we found in 1972.

11 My second point is the need to complete
12 what was begun in 1972 and not just -- not just the
13 tentative final monographs that are still languishing
14 in the Center, but rather a much broader program.
15 Completing those tentative final monographs is indeed
16 an important objective, and once again, it won't be
17 done without an office.

18 We also need to go back and look for the
19 products, and we know they are there, that fell
20 through the cracks in the early days of the OTC drug
21 review. I'd like to commend the agency, for example,
22 for doing just that with plaque and gingivitis, a
23 category of products that clearly did not get
24 addressed and was then readdressed most recently in
25 the early Nineties with a separate panel. That was a

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1 superb way to do it, and that model should be used.

2 Third, as the third sort of leg of this
3 stool, we need to take a look at are we serious about
4 bringing foreign OTC drugs into the United States
5 market. If so, you ought to tear up the December 1999
6 proposed regulation which was designed more to
7 preclude that from happening and to replace it with
8 the kind of open procedure that worked so well in the
9 OTC drug review.

10 Now again, all of these require people who
11 have the authority, resources, and responsibility and
12 commitment and mandate to do this, something I don't
13 think any of those exist today.

14 My third point is the need to convert
15 longstanding over-the-counter drug New Drug
16 Applications into OTC drug monographs. The whole
17 concept of switching changed in the early 1990s -- I'm
18 sorry, 1980s -- I misspoke -- with probably Ibuprofen
19 where the change was from the OTC drug review
20 monograph system to the use of supplemental or full
21 NDAs for this process.

22 A lot of those are now 20 years old.
23 There is simply no need to continue to submit
24 abbreviated New Drug Applications, Supplemental New
25 Drug Applications for every minor change in labeling

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1 or in the manufacturing methods. This is an enormous
2 burden on industry. It's an even worse burden on the
3 Food and Drug Administration.

4 It's the classic example of a short term
5 investment that is needed by the agency to get these
6 out of the NDA system for a tremendous long term
7 benefit of being able to spend your resources on more
8 important things like switch.

9 Now let me get to the fourth point. The
10 fourth point deals with the need to focus on
11 appropriate switch candidates, and I'm going to divide
12 my remarks into two categories. The first is what we
13 learned in the 1970s and how we did it. It doesn't
14 mean it's right, but it, I think, was quite
15 successful. The second is events that have occurred
16 more recently.

17 Let's go back to the 1970s. No category,
18 no type of drug, no type of indication was ever taken
19 off limits in terms of consideration of whether it was
20 a potential candidate for OTC status.

21 I briefed every single one of the 17 OTC
22 drug panels, and I told them open up your mind; think
23 of what is possible. We may or may not be able to
24 accept it, but don't take anything off the table until
25 you've thought it through on an individual drug by

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1 drug basis.

2 There is absolutely no reason under the
3 statute to set arbitrary, rigid rules and limits on
4 this process. No drug should be simply not
5 considered.

6 Now you hear all the time, OTC drugs are
7 palliative, not curative. That's nonsense. You hear
8 about acute versus chronic use. We have chronic use
9 OTC drugs now, and I heard Sid Wolfe, my good friend
10 Sid Wolfe who I debate often, make the same mistake
11 that people make all the time, that the hallmark of an
12 OTC drug is self-diagnosis. It is not, and never has
13 been self-diagnosis.

14 It is self-treatment. The concept of
15 physician or professional diagnosis followed by self-
16 treatment with OTC drugs is a long held concept, and
17 I would back to the first major discussion of that
18 that I recall was by Carl Peck when he was Center
19 Director in the mid-1980s.

20 So let's open up the concept, the
21 possibility. Now that doesn't mean all these drugs
22 will, in fact, be switched, but they should be
23 eligible for consideration.

24 Now on what basis do you proceed with a
25 switch? There are two possibilities. I firmly

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1 believe, and this was the way it was done in the early
2 1970s, that you proceed on the premise that patients,
3 consumers, are intelligent, educable, interested in
4 their own health, and want a share of their health
5 care decisions.

6 One could proceed on the basis that they
7 are unintelligent, uneducable, and that we ought to
8 ignore their interests and subject them to a doctor's
9 decision. Now that is a difference in philosophy.
10 Needless to say, you know which way FDA went in the
11 1970s.

12 The hallmark of the OTC Drug Review was a
13 collaborative, open process with pharmacists, doctors,
14 consumers, the regulated industry, all of the people
15 who had an interest, all of whom participated in the
16 ultimate decision. That decision was never once in
17 the ultimate, final endpoint disagreed with among
18 those parties.

19 Agreement because of the process, because
20 everybody was there working together in a
21 collaborative joint venture, we all ultimately reached
22 agreement. Let me say that again. In 30 years there
23 has never been a successful switch in which it was a
24 confrontation. It has always been a collaborative
25 collaboration.

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1 Now my time is up, and I, therefore, will
2 not talk about the more recent events except to say
3 that I applaud the agency for its attempts to make
4 better use of labeling, to require, for example, that
5 there be label comprehension and actual use studies to
6 reform the OTC drug label in totality, to begin to use
7 electronic means of communication that weren't
8 available to us 30 years ago when we were considering
9 this. But this just means that there are greater
10 opportunity to educate consumers and to bring them into
11 the process, to bring them into the individual
12 decision making on individual drugs on their own
13 merits.

14 So there is no limit, in my judgment, to
15 what could be OTC. There are clear limits to how to
16 go about it. Bob Temple, you said is it all right for
17 FDA to initiate discussion? Of course, it's always
18 all right for FDA to initiate discussion. But if you
19 get into confrontation, if you get into "we" versus
20 "them" rather than how to work this out together, then
21 I think the process will not work. Thank you.

22 MODERATOR DeLAP: Thank you very much.
23 You certainly have a unique perspective from your
24 unique involvement with this process over the years,
25 and it's very interesting.

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1 Do we have questions from the panel?

2 MR. HUTT: Thank you very much.

3 MODERATOR DeLAP: Thank you. We are going
4 to have a break now. It's about a quarter of four.
5 We are going to start up again promptly at four
6 o'clock. Thank you.

7 (Whereupon, the foregoing matter went off
8 the record at 3:44 p.m. and went back on the record at
9 4:05 p.m.)

10 MODERATOR DeLAP: Our first speaker for
11 the remainder of the afternoon session is Dr. John
12 Dent for SmithKline Beecham. Dr. Dent.

13 DR. DENT: Thank you. Good afternoon,
14 ladies and gentlemen.

15 In calling this hearing, the FDA have
16 asked a series of probing questions about the Rx to
17 OTC switch process, questions which to the casual
18 observer might indicate that serious issues exist with
19 the current process of switching products from
20 prescription to over-the-counter status.

21 SmithKline Beecham is a leading consumer
22 health care company which has been involved in Rx to
23 OTC switching since the 1960s. We are also in a
24 unique position to give a global perspective, as we
25 switch and market medicines throughout the world.

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1 It's the view of SmithKline Beecham
2 Consumer Healthcare that the existing statutes and
3 regulations, when employed in an open and
4 collaborative manner between the FDA and the sponsor
5 company, allow FDA to make determinations as to the
6 safety and effectiveness of products in the OTC
7 setting and to determine whether or not these products
8 can be properly labeled for use without the
9 supervision of a medical professional.

10 In employing the existing statutes and
11 regulations, we believe FDA should consider each
12 application on a case by case basis using the weight
13 of scientific evidence to make an informed
14 benefit/risk decision.

15 There are common issues which need to be
16 addressed in all switches. These are covered, for
17 example, in the UK Medicines Act, in the WHO
18 Guidelines, and in recently issued suggestions from
19 the EMEA, and they are comparable in principle to the
20 U.S. FDA-sponsor switch considerations. However,
21 there are specific questions which need to be
22 addressed with each individual switch.

23 On balance, we believe it's unnecessary
24 for the FDA to issue a broad switch guidance,
25 especially on an entire class of drugs or an entire

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1 therapeutic area. We support the need for a
2 collaborative approach where FDA works with the
3 sponsor company to identify the issues and to work out
4 acceptable ways to address them.

5 Working together, FDA and industry can
6 answer the public's desire for more opportunity for
7 self-care while appropriately managing the risk-
8 benefit equation for each proposed switch.

9 One of the best examples of the process in
10 action is the 1996 switch of Nicorette, nicotine
11 polyacrylics gum, to OTC status. Nicorette was the
12 first nicotine containing smoking cessation product to
13 obtain OTC status. The switch of Nicorette
14 represented a significant challenge for both the
15 sponsor and for the FDA.

16 I will briefly tell you how we addressed
17 the difficult issues that this switch had raised, how
18 we developed the data-driven solutions to these
19 issues, how by providing the agency with a post-
20 approval assurances we were able to address the issues
21 that could not be prospectively answered by facts and
22 data, and how the decision by the FDA to approve the
23 switch of Nicorette, which at the time was a
24 courageous decision, has led to substantial public
25 health benefit.

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1 I think at the end you will agree that
2 this switch resulted from an effective collaboration
3 between the regulator, the FDA, and the regulated,
4 SmithKline Beecham.

5 There were many issues that concerned both
6 the agency and us as the sponsoring company. Could
7 nicotine replacement therapy be as effective in the
8 OTC environment as it was as a prescription medicine?
9 Would the loss of health care professional involvement
10 in the process of smoking cessation reduce the number
11 of people trying assisted quitting or even reduce the
12 effectiveness of the product?

13 Nicotine is classed as an addictive agent.
14 Dr. DeLap pointed out at the beginning of this morning
15 that that was one of the specific exclusions for an
16 OTC product. Setting aside the obvious contradiction
17 that a highly addicting form of this drug, cigarettes,
18 was already available in general sale, there were many
19 who at the time questioned whether a medicine
20 containing nicotine could ever be made OTC because of
21 the addicting classification.

22 Many questioned whether diseases like
23 tobacco dependence with such a significant behavioral
24 component could be self-treated or whether a
25 physician's intervention and counseling was absolutely

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1 essential to achieve effectiveness.

2 Of great concern was how in an OTC
3 environment could access to the product be controlled
4 so that the product was not used inappropriately,
5 especially by minors.

6 The answers to these issues resulted from
7 a series of data driven solutions and from a set of
8 agreements between SmithKline Beecham and the FDA.
9 The OTC efficacy study demonstrated that Nicorette was
10 safe and effective in helping consumers quit smoking,
11 and that users were able to correctly understand the
12 label and to self-medicate.

13 The "real world" quit study demonstrated
14 that quit rates for smokers receiving Nicorette from a
15 physician not participating in a clinical trial were
16 not different from the quit rates achieved in the OTC
17 trial.

18 In the Rx to OTC switch process, consumer
19 research can be as important as clinical research. In
20 the Nicorette switch it allowed us to identify the
21 target population who were most likely to benefit from
22 the use of nicotine replacement therapy, a group we
23 termed committed quitters.

24 By targeting advertising preferentially to
25 this group, we were able to maximize efficacy and

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1 minimize the potential for misuse and abuse. Research
2 in teenagers clearly pointed to the fact that
3 Nicorette did not appeal to them as a substitute for
4 smoking nor as a product for the initiation of
5 nicotine dependence.

6 In addition to the extensive pre-approval
7 work that we did, SmithKline Beecham proposed 14
8 specific post-approval actions. These included: A
9 free behavioral program, training of doctors and
10 pharmacists who are the major players in the war
11 against smoking; surveillance designed to identify and
12 report on the sales and use of nicotine by people less
13 than 18 years of age, and we reported this information
14 quarterly to the FDA; age verification at point of
15 sale; targeting advertising to adult smokers;
16 voluntarily agreeing to no trial sizes and no sample
17 packs; targeting distribution to settings where OTC
18 drugs were sold, all measures designed to reduce the
19 risks associated with the availability of nicotine
20 replacement therapy over-the-counter and demonstrating
21 the ability to go beyond what is normally required for
22 an OTC drug.

23 The fact that we proposed and the agency
24 accepted these 14 specific post-approval actions
25 demonstrates the ability of a sponsor company to work

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1 with the agency. To tailor the marketing and
2 availability of an OTC product this way makes moot the
3 question of a third class of drugs.

4 Based on the data on the efficacy of
5 nicotine gum and the impact of increased access to
6 this therapy, the bold and difficult decision that the
7 FDA made in 1996 has had a huge public health benefit.

8 Based on the work by Shiffman, et al., it
9 is estimated that since the approval of Nicorette,
10 approximately 1 million people have quit smoking who
11 would not otherwise have done so. The benefits of the
12 switch of Nicorette gum were achieved, and the risks
13 were not realized.

14 So the current Rx to OTC switch process
15 works. It requires an open and honest dialogue
16 between the agency and the sponsor company. There is
17 no magic formula that works for all drugs. Each drug
18 must be considered on a case by case basis. Each will
19 have its own difficult issues, which can be answered
20 with data driven solutions.

21 Those questions which cannot be answered
22 prospectively can be addressed with post-approval
23 agreements or commitments from the sponsor, and in the
24 final analysis the public health benefit must occur.

25 I hope I've made a compelling case that

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1 the system can work. Using an example that falls out
2 of the usual expectations for an over-the-counter
3 medicine, I hope you will agree that the system does
4 not need radical overhaul.

5 Case by case, data driven solutions which
6 derive from a meaningful collaboration between the
7 agency and the sponsor are the key to ensuring
8 effective public health benefits resulting from Rx to
9 OTC switching. Thank you for your time and attention.

10 MODERATOR DeLAP: Thank you. Dr. Houn.

11 DR. HOUN: The post-approval assurances
12 program -- I guess a new term for them would be risk
13 management program, dealing with safety issues of the
14 drug. Did these come about as you were working toward
15 the switch or was it close to switchover time that
16 these things were discussed?

17 I just want to know if there are some
18 lessons learned on how to incorporate developing these
19 programs earlier on or -- your advice?

20 DR. DENT: I think the key is to think
21 about what the risks are, identify them, talk with the
22 agency about how to minimize them, put forward
23 proposals about how you are going to do that once
24 you've marketed the product, get the agency to agree
25 that that's appropriate, and then, most importantly,

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1 make sure you follow up on it.

2 MODERATOR DeLAP: Well, if there are no
3 other questions, thank you very much.

4 Our next speaker is Dr. Dunaway from
5 AMMSYS Research.

6 DR. DUNAWAY: Good afternoon. My name is
7 Gerry Dunaway. I am President of AMMSYS Research. We
8 are a contract research organization headquartered in
9 Annapolis, Maryland. Prior to my founding this
10 company, I spent 30 years with Proctor & Gamble.

11 As far as the hearing today, I represent
12 myself, and I'm not being compensated for this
13 presentation.

14 At the outset, I'd like to thank the
15 agency for scheduling these hearings, and especially
16 giving me an opportunity to speak. As way of
17 background of our company, we specialize in large Rx
18 to OTC switch studies. In the past 30 months, we have
19 completed seven larger OTC studies with a total
20 enrollment of 16,936 patients, marginally over 2200
21 enrolled in each study.

22 My comments today are directed toward the
23 agenda, that part of the agenda which is headed
24 consumer understanding, specifically the question of
25 how can the FDA be assured of consumer understanding.

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1 Now the reason I'm here is actually to
2 convey the importance of consumer -- or we believe
3 consumer research as a part of the current and future
4 switch decisions, especially when that research is
5 captured through a well designed use study.

6 In case Ms. Titus gets me with the time
7 hook here, let me switch to the conclusions and tell
8 you what our conclusions are, and then if I get in
9 trouble on timewise, at least you will go home knowing
10 what we thought.

11 There is no need for radical change in the
12 Rx to OTC process. We suggest that the Rx to OTC
13 switch process should be considered on a case by case
14 basis. Categories of products should not be excluded
15 from OTC consideration. Research should clearly drive
16 those decisions.

17 Rx to OTC should be viewed as a consumer
18 driven process. The FDA should consider -- seriously
19 consider accepting the principles of behavioral
20 science as valid research tools. FDA should frame
21 questions that the agency has concerns about and then
22 charge industry with the responsibility of finding
23 answers because, clearly, research techniques are
24 available.

25 Finally, use studies with appropriate

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1 design features can answer virtually all questions or
2 any question related to what the consumer will do,
3 specifically self-recognition questions, self-
4 selection and whether or not the consumer complies
5 with the label.

6 Now let me make four points on consumer
7 understanding or consumer behavior. First of all,
8 perhaps the definition should be given, and we're
9 talking attitudes, comprehension, and observational
10 research.

11 A more functional definition related to
12 clinical research might be the study of the consumer
13 in the decision process of selecting drugs in a retail
14 setting and, of course, the environment in which they
15 are acquired. Again, to restate, we think Rx to OTC
16 should be a consumer driven process.

17 Understanding consumer behavior is
18 essential to current and future switch decisions,
19 especially related to self-recognizable and self-
20 selection issues. Another way, what does the consumer
21 know? What can the consumer do, and what will the
22 consumer do faced with that product in a retail
23 setting?

24 We think, of course, as I've already
25 stated, that the best way to capture that information

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1 is through an actual use study.

2 There's a very strong case for consumer
3 behavior by examining the history of switch decisions.
4 We looked at the switch decisions over the last 20
5 years, and we divided them into three groups, and
6 these are just our headings, early, intermediate and
7 current.

8 We wanted to see what impact consumer
9 behavior had on each one of those periods. The early
10 phase studies, as you know, involved drug products
11 that provided primarily symptomatic relief and limited
12 public health impact. Consumer behavior was not a
13 defining issue.

14 The intermediate phase: Easily self-
15 recognizable conditions, heartburn, diarrhea,
16 baldness, again had a greater public health impact,
17 but did not require major self-selection decisions on
18 the part of the consumer.

19 Then the current phased switches, not as
20 easily self-recognizable, osteoporosis, high
21 cholesterol. It may require simple tests, have a
22 major, major public impact if they are approved, and
23 consumer behavior is just absolutely -- we think,
24 absolutely essential to these decisions.

25 Now in summarizing why we think consumer

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1 behavior is important and why we urge the agency to
2 adopt research techniques that will look at that is
3 that these complex questions associated with current
4 and future switch products must be -- the answers must
5 be driven by research.

6 Those questions must be framed properly in
7 open discussion between the FDA and the sponsor, and
8 research designs developed that will supply the
9 answers on which decisions can be made.

10 Let me talk for just a minute about actual
11 use studies. Dr. Bradford covered that very well, and
12 I compliment you on that. Let me talk -- Let me
13 summarize what I was going to say about actual use
14 studies by saying that essentially we agree with his
15 analysis of the use study.

16 We tend to talk about the static
17 traditional model, which is somewhat restrictive from
18 a recruiting standpoint, may not measure the real
19 universe, does not provide the consumer with an
20 opportunity to be the consumer and probably make the
21 decisions they would make in a store; and we see that
22 as very static and highly restrictive and not
23 appropriate, as it's designed now, to research
24 consumer behavior in the future.

25 We see an evolving model. There may be a

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1 better name for it, but that evolving model would
2 continue to do what a use study is designed to do, and
3 that's to answer specific safety and efficacy
4 questions. But it would also do a number of other
5 things.

6 It would be designed to answer consumer
7 behavior questions that we've talked about today and
8 that we all need to know. Be somewhat more
9 progressive in recruiting. It may be all comers. It
10 may be naturalistic, all of the buzzwords that we now
11 use for at least making or attempting to make sure
12 that the study sample represents the universe.

13 It has a real life retail environment.
14 It's somewhat less restrictive in measurements than
15 the current model, lets the consumer be the consumer,
16 and lets the consumer do what the consumer would do if
17 they entered a retail establishment to buy this
18 product.

19 It creates a self-selection environment,
20 and it provides maximum consumer flexibility. Our
21 experience -- and we have done a number of this type
22 study -- is consumers love it. They are more
23 comfortable. They are more relaxed, and we believe
24 their decisions are more in tune in this virtual
25 retail environment than it would be in any other

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1 environment you could put them in.

2 Now in conclusion and for purposes of
3 credibility, it's very easy to talk about these
4 issues, but I would like to review very quickly in the
5 remaining time I have a large switch study that we did
6 for the McNeil Consumer Healthcare, and you want to
7 guess what that's on.

8 You're going to swear there's a
9 competition gong on here, but it was on the Nicotrol
10 transdermal patch system. We really didn't -- No one
11 knew who was going to talk about what here.

12 We worked with Dr. Barbara Corberly in
13 running the study, and she said several things to us.
14 Number one is here's the way I want the study design
15 based on the protocol, but she also said we want to
16 learn as much as we can from the study about the
17 consumer. That's exactly what we did. She also said
18 we want to do that as quickly as possible.

19 Let me just run through the objectives:
20 To achieve a comparable efficacy in OTC and Rx arms.
21 This was a two-arm parallel OTC arm and conventional
22 Rx sites. Create virtual OTC retail environment.
23 Permit the patients to self-select, and there were a
24 series, which I don't have time to cover here, but
25 it's in the material that I handed out to the agency -

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1 - a series of consumer behavior questions that we
2 successfully measured.

3 This is a flow chart of the study. We
4 used primarily radio advertising. We thought that was
5 the best way to reach the large audience. They called
6 the 800 telephonic screening number, which is ours.
7 We screened them, randomized them, randomized to the
8 ten retail OTC sites.

9 These were actual stores in active
10 shopping centers, stores that we leased. We then
11 equipped them as an office, and we staffed them with
12 nurses or pharmacists or whatever is called for. On
13 the Rx side there were 13 physician offices.

14 This is a picture of some of them. I
15 think we have maybe three, and we'll flip through
16 those very quickly. You can see, they really are real
17 life permanent kind of retail establishments, and
18 those people who are randomized to the OTC site feel
19 that they are going into a real live retail
20 environment.

21 This gives you an idea of the summary of
22 enrollment. We generated, total calls in response to
23 the advertising, 14,809 calls, and that's quite a
24 burden -- not a burden, but it's quite a struggle to
25 answer the phone that many times.

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1 Out of that we enrolled 3385 subjects.
2 Out of the 3385, 150 failed to initiate treatment, and
3 in the study we had 3235.

4 Now just a word about the geographic area
5 we used -- I'm not sure, John. Do we have that slide?
6 We did something different on this, and again aiming
7 toward redesigning the use study to where it meets the
8 needs today, and it delivers the kind of answers
9 today.

10 We did that in one population area instead
11 of across the country with 30 or 40 sites, which you
12 would normally have for this kind of study. We did it
13 in a populated area of 5.9 million people, of which
14 1.2 million were smokers, and of that 1.2 million we
15 estimated fairly accurately that 120,000 were
16 motivated. That was really the study population we
17 were aiming for, for a sample size of 2500.

18 We ended up with 3385 enrolled and 3285
19 treated. The message today, and I see the red light
20 is really beginning to pick up tempo here -- Consumer
21 research is very, very important. It's very important
22 to your decisions today and your decisions tomorrow,
23 and I know you know that.

24 We see the use study modified, and there's
25 many ways to modify that, as the ideal tool for

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1 actually delivering the kind of information you want.
2 Now it does not -- Final statement: It does not
3 replace -- What we are saying does not replace the
4 comprehensive label study. That actually validates
5 what we find, the consumer research we find.

6 The label study tells us what the consumer
7 understands. The kind of consumer research we're
8 talking about tells us what the consumer will do when
9 they go into that store, if the product were sold
10 over-the-counter, the kind of compliance decisions
11 they would make, in tune with the label.

12 Thank you very much for this time.

13 MODERATOR DeLAP: Well, thank you, Dr.
14 Dunaway. Do we have questions?

15 DR. MURPHY: Could you tell us what is the
16 longest time in which you have involved the consumer
17 in follow-up in any of these studies?

18 DR. DUNAWAY: Can you be a little more
19 specific on follow-up?

20 DR. MURPHY: In other words, you're
21 talking about what they do, but then after they take
22 an action and they use a product or use it
23 inappropriately, is it days, weeks?

24 DR. DUNAWAY: It's a year. We follow up
25 for a year.

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1 DR. MURPHY: So your follow-up is the
2 longest has been a year.

3 DR. DUNAWAY: Yes.

4 DR. MURPHY: And the usual is -- Of the
5 seven studies, what was the usual time? All of them
6 for a year?

7 DR. DUNAWAY: The last seven studies? No.
8 Five of them -- Four of them were for a year. The
9 others were for six months, but they -- different
10 compounds. So like a smoking study, it's more
11 important. In fact, I think you require it when the
12 protocol is written that we follow six months and a
13 year. But we have not done a study where we do not do
14 follow-up.

15 Now, obviously, we carry out the protocol.
16 We don't write the protocol, but that's -- We
17 collaborate with our sponsors on that.

18 DR. MURPHY: And this is very interesting.
19 So I probably shouldn't take this much time. But in
20 that six-month follow-up, what percentage of dropout
21 to follow did you have?

22 DR. DUNAWAY: I'm sorry, I don't have
23 that. We could get that. I would have to, I think,
24 get the sponsor's okay to release that, but are you
25 saying, for example, in the smoking study what

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1 percentage of them would be abstinent at six months?

2 DR. MURPHY: How many of them were you
3 actually able to measure? Let's say you had 1,000 who
4 you randomized to your OTC site, and how many of that
5 1,000 actually were there at six months?

6 DR. DUNAWAY: In a different study, not
7 this study, we had very good follow-up. Approximately
8 60 percent of them we could reach. So 40 percent of
9 them were lost. They moved away or you couldn't get
10 back to them or they didn't answer the phone with
11 endless number of telephone calls to try to get them
12 back.

13 DR. MURPHY: Thank you very much.

14 DR. DUNAWAY: You bet. Yes?

15 DR. JENKINS: A couple of quick questions.
16 In these studies could you address how you've handled
17 the issue that a raised earlier about the self-
18 selection. If someone incorrectly self-selects to
19 enroll in the study and they have an obvious
20 contraindication, how have you handled that in those
21 studies?

22 DR. DUNAWAY: In all of these studies with
23 the exception of one, we said they self-selected, but
24 there were guidelines that defined consumers with
25 certain medical conditions that would not be accepted,

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1 pregnancy being one and other conditions.

2 So we have never done a study where -- Now
3 we talk about all comers, and I think we have to talk
4 about all comers, but there are shades of that. There
5 are certain medical conditions that, I think, our
6 position would be that you simply could not accept
7 everyone who comes to enroll in the study. Ethically
8 and medically, you could not do that.

9 DR. JENKINS: The second question I wanted
10 to ask is: Do you see any limitations to the ability
11 of this type of study to answer questions? Let me
12 just give you the scenario I'm envisioning.

13 For a lot of these chronic asymptomatic
14 therapies that people are proposing for over-the-
15 counter marketing, if the question the agency were to
16 formulate to the sponsor was, okay, show us clinical
17 benefit that your anti-hypertensive drug when used in
18 an OTC setting reduces cardiovascular risk, mortality,
19 morbidity, could you do a 100,000 patient OTC use
20 study for five or ten years?

21 DR. DUNAWAY: Well, we'd sure like to try.
22 You would expect me to say yes, and I want to be very
23 careful in using good judgment here. It depends --
24 Sure, you can. Yes, you can. There's no reason why
25 you can't. It costs a lot of money, but you can

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1 certainly do that.

2 In this retail sites that we have, there
3 are a number of benefits, and I don't want to give you
4 a sales presentation here, but you can either -- In
5 some cases, we've had doctors involved in the actual -
6 - at the site, pharmacists, research nurses. You
7 could keep them open 24 hours a day, if you want to,
8 because we own them. We own the lease.

9 If you want to bring people in the morning
10 before work or after work, it has a tremendous impact
11 on being able to -- we think -- our experience says,
12 on being able to get a balanced enrollment.

13 I'm coming to your point that you can
14 apply -- You can do whatever you want to do there.
15 We've even done studies where we -- involving blood,
16 and we have to get an okay for that, regulatory okay.
17 So the answer would be yes.

18 It would require a lot of coordination,
19 but yet if you contrast that to the logistics of a
20 100,000 patient study through a traditional Rx site,
21 it's probably more simplified and, my guess is, a
22 little more cost effective.

23 Again, if you know someone who is
24 interested, we'd sure like to talk to them. And I say
25 that with respect.

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1 DR. JENKINS: We just formulate the
2 questions.

3 MODERATOR DeLAP: Thank you very much.
4 Our next speaker is Dr. Frederick Sparling, Chairman
5 of the Infectious Diseases Society of America.

6 DR. SPARLING: Good afternoon. I do come
7 before you representing the Infectious Diseases
8 Society of America in my capacity as the Chair of
9 their Public Policy Committee and as former President
10 of the Society. We appreciate very much the
11 opportunity to address you here late in a busy day.

12 The IDSA represents more than 5500
13 physicians, scientists and other health care
14 professionals who specialize in infectious diseases,
15 and the mission of the Society is to promote and
16 recognize excellence in patient care, education,
17 research, public health and prevention of infection.

18 My statement concerns the IDSA's initial
19 comments to your notice concerning the approach to
20 regulating over-the-counter antimicrobials. We
21 ordinarily would have addressed this topic tomorrow,
22 but we appreciate the chance to speak to it out of
23 order today when we are available.

24 The IDSA strongly opposes changing the
25 regulations to allow antibiotics to be dispensed OTC

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1 without prescription from a physician, primarily
2 because it would increase the risks, in our opinion,
3 for additional development of antibiotic resistance.

4 There also could be other adverse effects,
5 including patient misdiagnoses of causes of apparent
6 infection, as well as drug interactions and
7 toxicities.

8 Antibiotic resistance is a clinically
9 significant problem at present and has been getting
10 worse throughout the world for many years. Indeed,
11 the problem has become sufficiently serious that the
12 public media have given much coverage to the emergence
13 of antibiotic resistance superbugs. It's hard to
14 avoid movies, television, radio, magazines that
15 discuss these problems.

16 These problems are particularly severe
17 within hospitals, but also increasingly involve common
18 outpatient infectious, in part due to shifting of care
19 to the outpatient arena. Patients have been infected
20 with bacteria that were resistant to every existing
21 antimicrobial agent and literally could not be
22 treated.

23 Fortunately, our good colleagues in the
24 pharmaceutical industry continue to be successful in
25 developing new drugs to treat resistant infections,

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1 but we cannot assume that this will always be the
2 case. We must do whatever we can to preserve the
3 effectiveness of currently marketed drugs.

4 Resistant bacteria are contagious, and a
5 single adverse event, rare as it might be, has the
6 potential to spread in an exponential way to other
7 contacts of the index case. The health of the public
8 depends on these decisions that you make.

9 Allow me to list just a few specific
10 instances for illustrative purposes. The
11 pneumococcus, the most common cause of community
12 acquired pneumonia and a common cause of middle ear
13 infections in children, meningitis and other serious
14 diseases, has gradually become resistant to
15 penicillins and other antimicrobials, including the
16 macrolides and trimethoprim and sulfas, and their
17 continued effectiveness in treating these classic
18 infections is severely threatened.

19 The gonococcus, a common cause of general
20 infections and a cause of fetal death and female
21 sterility, has become resistant to penicillins and
22 tetracyclines throughout the world, and is becoming
23 seriously resistant to fluoroquinolones.

24 The emergence of resistant gonococci and
25 pneumococci was noted first in areas of the world

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1 where antibiotics are freely available without
2 prescription. Many have concluded from these and many
3 other examples that development of resistance is
4 fostered by free availability of OTC antibiotics,
5 because this leads to use of inadequate doses and/or
6 abbreviated courses of therapy, both of which favor
7 emergence of resistance.

8 Any move to allow similar OTC distribution
9 of antibiotics and antimicrobials in this country
10 would undermine the public health safeguards that we
11 currently have in place to protect our citizens, and
12 place us on a par with lesser developed nations in
13 this respect. This would be a very serious step
14 backward.

15 There are many, many other examples of
16 similar problems. For instance, resistance of the
17 bacteria that commonly cause middle ear infections in
18 small children has increased dramatically in recent
19 years, and many believe this is the result of
20 inappropriate use of antibiotics to treat nonbacterial
21 upper respiratory infections. Over-prescription of
22 antibiotics by physicians, both in their office and
23 the hospital, is well recognized to be a problem.

24 IDSA is working with policy makers within
25 government and other societies to develop better

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1 guidelines and educational strategies to limit
2 antibiotic use to those situations where they are
3 really necessary.

4 If we accept that over-prescription of
5 antibiotics leads to emergence of resistance bacteria,
6 then anything that liberalizes the uninformed use of
7 antibiotics for nonindicated conditions would
8 aggravate the problem.

9 It could be argued that antibiotics might
10 be approved for OTC use for syndromes for which good
11 algorithms for treatment exist and in which diagnosis
12 is relatively simple, such as urinary tract infections
13 or diarrhea. However, inappropriate use because of
14 misdiagnosis still is to be expected.

15 OTC antibiotics might be restricted to
16 only certain common classes of drugs such as the
17 currently approved neomycin bacitracin for topical
18 use, reasoning that this should be unlikely to cause
19 problems of resistance to more commonly used
20 antimicrobials. However, this would not necessarily
21 prevent emergence of resistance to common used drugs,
22 for the reason that genes for resistance to different
23 kinds of drugs are commonly carried on single mobile
24 genetic elements or may result from a single mutation
25 in an efflux pump. Treatment, in other words, with a

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1 single drug may result in emergence of resistance to
2 multiple drugs.

3 The only safe policy is to restrict as
4 much as possible use of all antibiotics to situations
5 where informed evidence suggests they are needed. We
6 urge you not to approve further OTC distribution of
7 any antibiotic or antimicrobial agent for topical or
8 oral use in humans without clear and convincing
9 evidence that such a policy would not result in
10 selection for resistance to these or other
11 antimicrobial agents or an increased incidence of
12 important misdiagnoses or other adverse effects.

13 The IDSA looks forward to having the
14 opportunity to continue to work with you on developing
15 good public health policy. Thank you.

16 MODERATOR DeLAP: Thank you, Dr. Sparling.
17 Comments, questions? Dr. Murphy?

18 DR. MURPHY: When you state clear and
19 convincing evidence, some of the evidence that has
20 been presented to FDA is modeling. There is also
21 evidence from actual experience in other countries.
22 Would you give us your opinion of what you mean of
23 clear and convincing evidence?

24 DR. SPARLING: Well, there's all kinds of
25 evidence and all kinds of questions. So I don't know

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1 that I can give a generic, all inclusive answer that's
2 satisfying to me or to you.

3 In general, I'd like to see experiential
4 evidence as opposed to modeling evidence. I would not
5 personally want to exclude evidence from other
6 countries, were it well gathered under conditions that
7 we understand and with similar criteria for
8 evaluation, but evidence that informed observers,
9 unbiased, could look at and draw reasonable
10 conclusions from.

11 DR. MURPHY: This question has been asked
12 of a lot of people today. So I'm not going to let you
13 escape.

14 Would the use of a third process for
15 certain of these syndromes -- let's say, recurrent UTI
16 where one had an initial physician diagnosis and then
17 a third process, the learned intermediary pharmacist -
18 - would that be a system that the infectious disease
19 community would consider or feels we don't have enough
20 information to go that route, or you just think the
21 problem is so large we shouldn't do anything in that
22 direction?

23 DR. SPARLING: I couldn't stand before you
24 and say you should never consider something. I think
25 you're probably best advised to have an open mind, as

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1 others have told you.

2 On the other hand, I would urge you,
3 because of the unusual public health implications of
4 potential exponential spread of problems to other
5 people in the public as a whole with infectious
6 diseases, to have a negative bias and demand evidence
7 when proposals are brought forward.

8 With regard to the specific question of
9 UTI, I would argue that an initial diagnosis and
10 prescription with recurrent episodes in the patient
11 subsequently is a clear case where the patient does
12 need to go back to the physician and not to be treated
13 over-the-counter, because it is very likely, if there
14 is either an anatomical problem or a resistant
15 infection, something is wrong.

16 So that's an easy answer. That would be
17 an inappropriate use of such an under-the-counter
18 strategy.

19 MODERATOR DeLAP: Now Dr. Cantilena?

20 DR. CANTILENA: Yes. Dr. Sparling, just
21 a couple of quick questions. So you're not saying
22 that there is absolutely no indication or infection
23 that should never be over-the-counter? It's just --

24 DR. SPARLING: No, I would not say that.
25 Indeed, we have neomycin polymix, and it works. There

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1 are no problems. And as far as I know, topical
2 therapy for vulvovaginal candidiasis is not causing
3 lots of problems, and it may very well be that there
4 will be topical microbicides for general tract
5 infections that will be very important.

6 So I don't think we can say categorically
7 that it doesn't work now, and it won't work in the
8 future. But there are very great risks of allowing
9 wider use of drugs, as has been done in so much of the
10 world, with very, very bad consequences for the public
11 as a whole.

12 DR. CANTILENA: And just another question.
13 Your premise is that -- I'm just trying to understand.
14 Are you saying that, in terms of self-therapeutic
15 concentrations and abbreviated courses of therapy,
16 that that does not occur with prescription
17 antibiotics?

18 DR. SPARLING: Oh, no, I didn't say that,
19 because it does occur, and compliance is imperfect, as
20 we all know. But I would also argue that it is more
21 common if antibiotics are self-prescribed and traded
22 on the street.

23 DR. CANTILENA: But how do we know that?

24 DR. SPARLING: Well, there's not
25 controlled prospective trials. It is an educated

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1 opinion on the basis of a very large population of
2 physicians who work in this area that it is so, and it
3 is drawn primarily from the experience that resistant
4 bacteria -- This is certainly true -- have emerged
5 first and are more prevalent in areas of the world
6 where, among other factors, oral antibiotics are
7 readily available over-the-counter and are commonly
8 traded among people after very short courses of
9 therapy.

10 That doesn't prove it, but it's the best
11 we have, and we have to make informed judgments. My
12 judgment is that it's likely to be a cause for why
13 we've seen these problems emerging in those countries.
14 I believe that's exactly how one does it in the
15 laboratory.

16 MODERATOR DeLAP: Dr. Kweder.

17 DR. KWEDER: Earlier today -- I'm not sure
18 if you were here to hear those comments -- we heard
19 from several speakers that decisions about OTC -- in
20 the case of OTC switches on the part of the agency,
21 for the agency to try and make public health
22 assessments and take those into account in granting
23 switches is beyond the purview of the FDA, that we
24 shouldn't be making public health assessments.

25 I would gather from your comments that you

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1 see that differently.

2 DR. SPARLING: Yes. I don't see how one
3 can deal with a situation, especially, let's say, of
4 communicable disease without considering the innocent
5 partners or contacts of the index patient who become
6 infected and then are not treated. We could cite so
7 many examples, multiple drug resistant tuberculosis
8 and on and on and on.

9 So it is important and should inform
10 policy.

11 MODERATOR DeLAP: One other thought that
12 we don't have so much control over, but seems to
13 overhang this discussion, that we can be very virtuous
14 and fastidious in our approach to these issues, and
15 yet when there are large parts of the world and other
16 ways in which these products are being used, clearly
17 the infectious agents do develop resistance, and they
18 are transmitted around the world then.

19 Are there any other things that we could
20 think about or ways that we could advocate or
21 anything, leverage, anything to try and keep these
22 drugs useful longer, so that our pharmaceutical
23 industry doesn't have to keep coming up with a new one
24 every couple of years?

25 DR. SPARLING: Is that a question to me?

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1 MODERATOR DeLAP: Yes.

2 DR. SPARLING: There are many things that
3 might work, but I think the thing we know the best is
4 that judicious use when indicated only, for the right
5 length of time with the right dose, is the best thing
6 we can do. Indeed, when resistance has become an
7 overwhelming problem, the ways it's been managed is
8 very assiduous attention to giving the right drugs in
9 the right way by directly observed therapy in the case
10 of tuberculosis or, let's say, in in-patient units to
11 restrict the use of antibiotics or to close the unit
12 and stop the antibiotics, at which point the bacteria
13 revert back to sensitivity again.

14 So taking the pressure off of them or
15 treating them broadly to really get them all are the
16 only ways to really manage the problem, that I'm know,
17 and a little bit of antibiotics here and there is what
18 leads to the emergence of resistance.

19 MODERATOR DeLAP: It sounds like we should
20 do our part and hope that others will do enough of
21 their part that it will work out well enough.

22 Okay. Well, are there other questions?
23 If not, thank you very much.

24 We'll continue to Warren Pinchert of
25 Cholestech Corporation.

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1 MR. PINCHERT: I'm going to be running my
2 own slide show here. So I'll try and speak up.

3 Well, the bad news is that I'm your 3:30
4 speaker, but the good news is there's only one left
5 after me.

6 I'm here today representing Cholestech.
7 We are a publicly owned company on the West Coast.
8 That's why I'm the only person here and running the
9 only slide -- my slide show by myself.

10 Our goal is to provide convenient,
11 accurate risk assessment for certain chronic diseases,
12 and also to provide tools to help people reduce that
13 risk, and then also provide convenient monitoring of
14 the progress of that treatment.

15 I'm sure you are all aware that there is
16 a lot of technology that is rapidly developing that
17 allows for more effective personal health management.
18 I think we have to look at three different things as
19 far as technology.

20 One is, obviously, the diagnostic piece of
21 the equation, and then the method of testing and how
22 wide and how easy that access is to the general
23 public, and then what kind of tools are you going to
24 allow the individual consumer to have to monitor their
25 progress.

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1 The diagnostic part will stratify your
2 risk so that you know whether you should be just
3 improving your lifestyle or whether you should
4 possibly be on an OTC medication or whether you should
5 go see your doctor and be on a prescription drug.
6 There is technology today that allows that
7 stratification.

8 The national testing will allow access of
9 venues that are convenient to the ordinary, everyday
10 person, so that they don't have to get up at seven in
11 the morning and go down to the hospital lab to get a
12 venous draw of blood.

13 They can go to Wal-Mart, Walgreen's and
14 get an accurate and precise reading and risk
15 assessment at a place that is convenient to them, and
16 then the ability to get tools offered to them so that
17 they can improve their lot in life.

18 Now, obviously, you've already guessed
19 from the name of the company that Cholestech deals in
20 cholesterol. There are a lot of other diagnostic
21 pieces of equipment out there that address chronic
22 diseases, but I know, obviously, that Cholestech
23 L.D.X. is the best. So that's what -- At the risk of
24 being commercial, I'm going to talk about that today,
25 because I think, if you just forget about the L.D.X.

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1 and think about what I'm going to talk about as the
2 delivery system, I think that's really what is
3 important.

4 Now the Cholestech L.D.X. provides a full
5 lipid profile on a single drop of blood in less than
6 five minutes. That means you get total cholesterol,
7 HDL cholesterol, triglycerides, a calculated LDL, and
8 we can also do glucose on that same drop of blood.

9 So you can have within five minutes an
10 accurate assessment of the person's cholesterol
11 reading, and then as long as you are addressing the
12 other risk factors for coronary heart disease, you can
13 evaluate somebody's risk and point them toward their
14 doctor. That is what I mean by technology on the
15 diagnostic side becoming more accessible to people.

16 We shipped over 3.5 million tests last
17 year. So it's not like this is just starting. It's
18 already out there in the marketplace.

19 One of the things that is driving quality
20 in this area, and as coming from a diagnostic company
21 it's hard for me to speak up for CLIA, but I've got to
22 be honest and say that having to go through the pains
23 of getting a product waived under CLIA certainly has
24 improved our product; because if you focus on the last
25 bullet there, we had to do additional clinical studies

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1 beyond what is required in a 510(k), and we had to
2 prove that our product was accurate and precise at
3 medical decision points.

4 Now, obviously, for cholesterol, you know,
5 that's 200, 240, but there are other technologies that
6 address osteoporosis and asthma. So those are already
7 on the market.

8 This is very important when you talk about
9 extending the reach to consumers and in the discussion
10 today, because if somebody is going to make a decision
11 on an OTC product, they need to have an accurate risk
12 assessment at the point where they are going to
13 purchase that product, not away from the decision but
14 right there.

15 The national testing: Cholestech on its
16 own is being used at General Motors, Sears. It's been
17 used at Walgreen's, all kinds of different locations.
18 But Cholestech has recently started a national testing
19 service called WellCheck.

20 The goal there is to have an approach to
21 testing that is the same quality across the United
22 States at whatever site you go to, and this is all
23 chronic disease related. So that when somebody goes
24 in in California and has their cardiovascular risk
25 assessed, that is the same assessment as they will

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1 receive in Maine. That is the goal of WellCheck.

2 We will have consistent high quality
3 service, and the results will be treated the same
4 across the United States. The goal is to have this
5 free to the individual.

6 What that means is Cholestech is not going
7 to make any money on the testing service, but we want
8 the other cholesterol interested parties to be able to
9 offset the cost of testing the people out there. That
10 way, more people become aware of their cardiovascular
11 risk and can be directed to their doctor and evaluated
12 appropriately.

13 You can tell I haven't done this a lot.
14 You have to bear with me.

15 The last part of our chronic disease
16 system is actually a Website, and I invite you all to
17 log on, wellcheck.com. It is clearly cardiovascular
18 oriented at the moment, but we plan to add other
19 disease states, chronic disease states, as we go
20 forward.

21 The content from this site was developed
22 by Stanford, their Center for Disease Prevention, and
23 we also use the NCEP diet planner and other things
24 from that agency on the Website.

25 Somebody will be tested -- Let's say we

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