interview

# Jerome Skelly on regulation, education and information

Interviewed by Samantha Barton and Ariel Retik



**Jerome P. Skelly**
***President, American Association of Pharmaceutical Scientists***

Jerome P. Skelly is the 2005 President of the American Association of Pharmaceutical Scientists (AAPS) and Adjunct Professor of Biopharmaceutics at the University of Cincinnati College of Pharmacy. Skelly received his undergraduate degree and his PhD in Chemistry from Wayne State University in Detroit and completed a post-doctorate in Pharmaceutics at the University of California at San Francisco. He held senior scientific and management positions in the FDA for more than 24 years, much of it as director and program manager for biopharmaceutics. He was also a World Health Organization consultant to Egypt. At the time of his retirement, Skelly served as a member of the Senior Executive Service of the US Federal Government, holding joint appointments as Deputy Director of the Office of Research in the Center for Drug Evaluation and Research and Associate Director for Science in the Office of Generic Drugs. Throughout his career, Skelly has received notoriety from AAPS for his contributions to pharmaceutical science, including being selected as an AAPS Fellow and awarded the 2002 AAPS Distinguished Service Award.

***Can you tell me a bit about yourself and your career to date?***

After my army service, I returned to school to get my PhD from Wayne State University in Detroit and then a post-doc in pharmaceutics at the University of California under Malcolm Rowland. After that, I joined the Bureau of Medicine in the FDA – now called the Center for Drug Evaluation and Research (CDER). I arrived shortly after the law changed requiring the FDA to establish a drug's efficacy as well as its toxicity. Up until that time, it was largely an inspectional body, so they had all kinds of problems – both political and scientific, especially with trying to determine the efficacy of drugs. At that time, the agency was directed to decrease the cost of drugs in this country, and was therefore pushing generics. I knew that there were problems with some of the generics in the marketplace, therefore got involved with these issues and helped to solve a number of them. After that, I headed up the biopharmaceutics program in the FDA, which addressed drug product bioinequivalence issues and aided the establishment of the generic drug program. When I retired from the FDA, I assumed a position as executive vice-president of research in industry. I am a former chairman of the board of the Product Quality Research Institute, and I am presently the president of the American Association of Pharmaceutical Scientists (AAPS). I also have an adjunct appointment of professor in the College of Pharmacy in the University of Cincinnati.

***What does your day-to-day role as president of the AAPS involve?***

I head the AAPS Executive Council and communicate with the executive director on routine administrative, legal and financial issues. We work together to develop our monthly executive council agendas. As president, I am also the chief executive officer and communicate with the membership through the AAPS news magazine. I work with staff on scientific issues and I am available for interviews with the press as necessary. I also have special obligations during our annual meetings, we now have two: a biotechnology meeting in the spring*, and an annual meeting in the fall. It's much more active than I anticipated!

***In your inaugural speech as president of the AAPS, you described a program called 'Getting the Dose Right' (which is a collaboration between the AAPS and the FDA). Could you tell us a bit more about the specific goals of that program?***

*The AAPS National Biotechnology Conference will take place on 5–8 June 2005 in San Francisco, CA, USA.


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This is a very interesting issue. There are two reports, one by the World Health Organization (WHO) and the other is a publication by the FDA that was in-part authored by the then-director of CDER, who was my immediate superior when I was there. Both of these reports had to do with significant reductions of doses for drugs that were new chemical entities. The WHO noticed that while there were a number of dose increases after a drug product was approved, there were a significantly higher number of dose decreases. When the FDA examined the issue they looked at products that had been approved within a certain interval by the FDA and found that 21% of these new medical entities actually had a change in dose, and that 79% of these were safety-motivated dose reductions. This is a significant issue – whether or not the FDA got the dose correct or whether the industry got the dose correct. The AAPS is currently working with the FDA and key leaders to develop a workshop on this topic.

*'…there is disagreement about the robustness of the data.'*

***You are a strong believer in science-based regulation. How do you think this can have an impact on getting the dose right?***

There are several positions on this issue. Some medical officers in the FDA are arguing that the paper published by the FDA was incorrect, and there is disagreement about the robustness of the data. One of the things that the AAPS stands out in as a professional association is that we can bring people together. You can argue these things for years in the literature, but the best thing to do is to bring academia, industry and the FDA together in a major workshop where you have the very best people putting their proposals on the table. Everyone is then free to argue their various points of view and tries to develop a consensus so that the issue can be resolved or at least have narrowed its focus. That's basically what we're trying to do here.

***Do you see a significant drop in the number of students continuing their education and entering postgraduate research in the pharmaceutical sciences?***

What we've seen here in the USA is a decrease in the number of pharmacy students that have gone on to graduate education. Some schools of pharmacy now give a doctorate in pharmacy rather than just a bachelor's degree in pharmacy – I think that went along with the development of what we call our Pharm. D. program. This has been true for the past two decades in our graduate schools of pharmacy, but we've actually found that the opposite is true for the other disciplines. AAPS has had an increase of over 15% in student membership over the last year, and our members now include students from 35 countries and 100 universities. At the same time, we know that there is a lack of recruitment – that is especially true in the areas of drug formulation and drug development. We have a proposal that has been developed by one of our sections, the pharmaceutical technology section, to address this issue, which we have referred to our student post-doc outreach committee and executive council.

*'Everyone is then free to argue their various points of view…'*

***You were a WHO consultant for Egypt. Can you tell us about this role?***

I went as a WHO consultant to try to help them develop regulatory programs. We already had sophisticated programs in this country and rather than have them go back to square one and create a plan from scratch, someone like me could provide assistance in developing a system for drug monitoring and development. I also worked with the minister of health and the director of the National Organization for Drug Control and Research, their equivalent of the FDA, to help in the development of their regulatory program. When I was in Egypt early last spring I, along with some other colleagues, inspected a number of pharmaceutical firms and I was tremendously impressed at the quality and the improvements that have taken place. As a matter of fact, many of the Egyptian firms are trying to make drugs to EU standards so that they can sell them in the European marketplace. This has resulted in a tremendous improvement for Egyptian public health.

***What is your opinion on the issue of making prescription drugs available to developing countries at reduced costs?***

I think that this issue has some tensions. There are people in the USA, particularly among the elderly, who feel that they are paying much higher prices for the same product that they can purchase overseas or in Canada for less. I think that there are political, economic and regulatory overtones to this, and society, at least in the USA, needs to address this issue. On the other hand, I note that there are a number of pharmaceutical companies and international organizations that have made excellent strides in this area and are really helpful to the neediest countries. I think this is a real step forward, and of course the AAPS stands ready to help in any way it can.

*'…they are paying much higher prices for the same product…'*

***In February 2004, the FDA released a report on how to combat counterfeit drugs in the USA, and this was one of the hot topics covered at the AAPS meeting in 2004. What do you see as the biggest issue in this area, and do you think there is anything else that can be done to combat the problem?***

This is an issue related to developing technology. I have colleagues who are actively working on this. We see an interest in developments like radio frequency identification or RFID, and I know that some firms, like Purdue Pharma, made a combination product to make OxyContin much less desirable to be abused and therefore counterfeited. There are other developments in this area and the science is still in an early stage. AAPS is actively pushing programs to address this issue and facilitate the development of these technologies.

***You were Associate Director for Science in the Office of Generic Drugs. Do you think that the public is still unsure about the safety and efficacy of generic drugs? If so, what more do you think can be done to improve public perception of these treatments?***

The FDA has a feature on its consumer education website, called 'Frequently Asked Questions', that tries to explain to the public

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that these drugs really are effective and bioequivalent. Now, about 50% of the drugs that are prescribed in the USA are generic drugs. It's a huge volume. And I can tell you from my time as an FDA insider, from my time in the industry and also as a professor of biopharmaceutics, that a number of firms tried to show that generic products in the marketplace were not bioequivalent. I had to deal with a lot of that data when I was in the FDA and can tell you that since 1972, when I got involved in the program, that of all the products in the USA that have FDA approval and meet all of the US Pharmacopoeia specifications, not a single batch has been determined not to be bioequivalent. That's a tremendous record, and one I am absolutely delighted with, because I had a hand in developing it.

*'…not a single batch has been determined not to be bioequivalent.'*

***Do you think all the data generated from clinical trials, both industrial and academic, should be made public?***

AAPS carried out a survey of members in the Baltimore meeting [7–11 November 2004], and found that our association, which has representatives from government, industry and academia, is evenly divided on the issue. About 47% said yes and 53% said no. Part of this issue, I think, has to do with definitions, because when you dig down into the data, the question really is: what was the purpose of this particular clinical study? Sometimes it is just to develop a new dosage form, sometimes it is to really see if there is any effectiveness in an early trial, sometimes it is to try to establish the dose where toxicity begins, All of these issues come in to play, It is not just a yes or no answer, it is more complicated than that. But it is quite clear that there is an even split in the thinking on this issue.

***Going on from that, do you think that unsuccessful data should also be considered as part of the approval process? Should the issuing of permissions for future studies depend on the complete publication of the previous study?***

I think that the term unsuccessful data really needs to be very carefully defined. Many people will, for instance, make a capsule as the dosage form that they study in their investigations, but then marketing people say 'Hey, you can't sell a blue capsule, it has to be a pink tablet, it has got to have a score and it has got to have an R on it'. A bioequivalence study should be conducted and if that fails because you have compressed your tablet too hard – that's a failed study. That is not going to be something you are going to be marketing, you are going to change the tablet compression and conduct the study again. The question really is: was the study improperly designed? Was this an exploratory study? There are a whole series of issues that need to be resolved before you can come up with a yes or a no.

***How do you think the confidence in the pharmaceutical industry has been affected by the recent problems with some approved drugs, for example, the cyclooxygenase (COX)-2 inhibitors?***

The COX-2 case is an interesting one and brought a lot of issues into the limelight. The FDA review process is the most comprehensive one in the world, but, unfortunately, the FDA has to operate under the laws that are enacted by Congress and under the budgets that Congress gives them. If Congress really wants the FDA to monitor these studies more closely, it needs to provide them with the financial and authoritative resources to do so. I really feel, as an individual – I am not speaking for the association – that Congress needs to do more on this issue.

*'The FDA review process is the most comprehensive one in the world…'*

***What do you think that your greatest career achievement is to date, and what you are perhaps most proud of?***

There are really two. One was when I first started in the FDA, my mentor was an MD–PhD, who had us study endocrinology and biology, as well as chemistry. We were focused on quantifying medical phenomena, which provided me an excellent basis for dealing with the problems I was to face in the FDA. When I joined the agency in 1968, there was a doctor in Alabama who found a baby with maple syrup urine disease. Maple syrup urine disease is a disease where the child cannot metabolize branched-chain amino acids so these accumulate in the blood, eventually spill out through the kidneys into the diaper and it smells just like maple syrup. This doctor was extremely shrewd, and he diagnosed this infant right away, contacted the FDA and said 'Get me some milk formula that doesn't have these amino acids'. But the FDA did not know how to handle this request, and finally assigned it to me, a brand-new employee at the time. When I looked at it, I was furious, because a considerable amount of time had passed and nobody had done anything. That particular child died. I involved a senior pediatrician who was an absolutely wonderful woman, really well-trained, and a MD who was the head of our food office. The three of us, along with Frances Kelsey, who stopped the approval of thalidomide in the USA, got together and set up a program so that any physician who diagnosed a case of amino acidurea could go to a poison control center to obtain the amino acids they needed. That solved the immediate problem and those who dealt with the issue eventually formed a professional society. I am really proud of this. My other major accomplishment is what I did in the area of bioequivalence and dissolution. Because of the regulations we developed, we no longer see bioinequivalent products in the USA. And I am absolutely delighted with these results.

***Who or what has been the greatest influence in your career?***

That's a tough one. In addition to my parents and wife, who were very supportive of me, I would have to say Frances Kelsey, because she was such a really great person, J. Richard Crout, who was the director of the Bureau of Medicine when I joined, and Sam Fine, who was the associate commissioner for compliance and the top civil servant in the FDA. Each one of these three people were people of integrity, they had principles, and they were superb scientists who insisted on good regulations based on science. That idealism and morality have always nourished me. Whenever I make a really tough decision, these three people pop into my mind.

***What would you like to have accomplished by the end of your term as president of the AAPS?***

# biotech focus

First, I would like to improve the effectiveness of our scientific workshops and review the operations of our scientific focus groups. We are also working to increase the number of student chapters and student membership, since students are the future of our association. I am also looking to increase the value of the association to our long-time members – we have responded to our members' needs by adding the annual AAPS National Biotechnology Conference, and it is one of my goals to expand and enhance this meeting. I'm especially focused on communication and publication. Right now, if you really want to get targeted scientific information on an ongoing basis, you have to join a particular scientific society and subscribe to their journal. We have now established several open access electronic journals so you don't have to be a member of AAPS to gain access to them. We also have a comprehensive plan that addresses something we call 'distance learning'. I am very interested in this because we might have an important workshop in the USA, for instance, the one on getting the dosage right, and 300–500 hundred people attend. But what happens to people in Western Europe, India, Egypt or wherever? They are not part of that. If you have a good distance learning program, these workshops can be put on the web and made available immediately across the world. Sharing this information could improve the lives of a lot of people.

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## A viewpoint on South Korean Biotech

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Like many other countries in the region, South Korea regards biotechnology as an important area for investment over the next decade. The country has high ambitions for this sector, but its growth depends on an environment that encourages innovation in research and that provides adequate funding of such ventures.

The emphasis on biotech in South Korea is influenced by the outstanding success of the US biotech industry – an economic feat that most other countries would like to emulate. In 1992, revenues from the US biotech industry totaled USD$8 billion, by 2003 this was close to USD$40 billion. There are now 1,473 companies operating in the US biotech industry [1], which illustrates how the conditions for the sector have improved despite the continuing difficulties and expense of drug development. In 2003, the US biotech industry spent USD$17.9 billion on R&D [1], which puts it far ahead of any foreign biotech industry [2]. This commitment to research has made US biotech companies the most successful in terms of new products. Companies such as Genentech, Amgen, Biogen, Chiron and Genzyme have performed impressively over the past 20 years and have brought to market important therapeutic products. An additional benefit for the US sector is that its success attracts those seeking to work in the field. For example, many foreign students, including many from Asia, wish to gain experience working for a US organization.

Matching the success of these US industry leaders is a problem for the young biotech companies in South Korea, as they are operating in a very different environment and at a later stage in the development of the global industry. Funding has always been a problem for biotech companies and investors are much more circumspect about investing in new ventures than they were two decades ago. This is particularly true for South Korea, where the 1997 economic crisis severely dented the country's growth prospects and led to foreign investors selling their assets.

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