Vaccine**Viewpoints**

Predictions and case studies
to help drive your business

The vaccine business is changing

From an increasing focus on immunotherapy, to new methods for formulating vaccines, to changing partnership models between all major stakeholder organizations there is a lot going on which could significantly impact your own company. Whether you are already waist-deep in late-stage trials or you are still in the pre-clinical validation stage, it is more essential than ever to be aware of what is going on outside your labs.

Throughout this book, leaders in the vaccine field from big pharma, biotech, non-profit, academia and leading suppliers have opened up to VaccineNation regarding what they are working on, their hottest predictions for the next 12 months and even what their last vaccine was.

Georgia McCollum
Georgia.mccollum@terrapinn.com
+44 (0) 207 092 1158

Dr. Niranjan Y. Sardesai
Chief Operating Officer
Inovio Pharmaceuticals

Prediction for the next 12 months:

In the pharma industry as a whole, and so within the vaccine industry, there's a lot of consolidation. I think that's going to drive some of the excitement in 2014.

From a broader, holistic aspect, vaccines have traditionally been looked at as preventative or prophylactic, but I see the focus shifting or greater attention being paid to therapeutic vaccines and immunotherapies.

Last vaccination...

Influenza.

VIEWPOINT:
DNA Vaccines

What is the potential for DNA vaccines across a broad range of cancer indications?

There's a good chance we'll look back at the next 10 years and see them as the decade of DNA vaccines. There have been some key scientific papers and developments in the field that all point towards important breakthroughs in enhancing immune responses and then enhancing both the quality and magnitude of immune responses that DNA-based vaccines have elicited, in a wide variety of model systems as well as in the clinic.

In addition, DNA has long enjoyed a strong safety record in comparison to other viral vaccine approaches. The challenge has been to translate that safety profile into meaningful efficacy profiles to both treat and prevent hard-to-treat diseases, like certain infectious diseases and cancers.

From a cancer perspective, what makes DNA-based vaccines exciting is that we've been able to show we can break tolerance in a number of different animal models. In humans, Inovio and others have now shown that you can generate robust and durable T-cell responses, both CD4 and CD8.

Coupled with these advancements, another exciting development is the emergence of "checkpoint inhibitors" – PD-1 and PDL-1 antibodies – which researchers have employed to try to take the brakes off the cancer immunotherapy area. Whether it's BMS' work or Merck's work, to name just a couple of leading companies, what they've shown is that T-cell responses are essential for dealing with cancer.

In September, Roche signed a $400 million deal with Inovio to co-develop Inovio's DNA vaccines for prostate cancer and hepatitis B. Overall it's a validating event for the broader DNA vaccine field.

Dr George Siber
Executive Director and Chairman of the Scientific Advisory Board; Chief Scientific Officer
Genocea Biosciences, Inc; ClearPath Vaccines

Prediction for the next 12 months:

In December, *Science* named Cancer Immunotherapy as the Breakthrough of the Year. The technologies underlying the recent successes with monoclonal antibodies against checkpoint inhibitors for T-cell responses, such as CLTA-4 and PD-1, will be applied to vaccines, not only for cancer but also for serious chronic infections such as hepatitis B, hepatitis C and HIV.

Also, advances in structural biology will enable us to develop much more effective vaccines such as an RSV vaccine containing the key fusion protein in its pre-fusion conformation, broadly cross-neutralizing influenza immunogens and perhaps, the holy grail of HIV vaccine research, broadly cross-reactive antibodies for HIV followed by immunogens which can elicit them. Increasingly we will see applications for vaccines that move beyond infectious diseases, such as allergies and autoimmune diseases.

Lastly, discoveries of better and safer adjuvants and other immunomodulators and targeted delivery of those adjuvants to the immune system, together with the antigen using technologies such as nanoparticles, will enable safer and more powerful vaccines.

Last vaccination...

I had the high-dose flu vaccine about 2 months ago.

VIEWPOINT: Pharma/Biotech Partnerships

How do you see partnership models changing in the coming years between pharma and biotechs?

Currently one of the ways large pharmas reduce the risks and costs of performing vaccine discovery and early development in-house is by in-licensing technologies from academia and biotech companies. Generally this will cover products that have already entered clinical stage and preferably have some clinical evidence of efficacy.

Vaccine biotechs also face challenges, in terms of managing costs and obtaining funding. An attractive option is to evolve a virtual vaccine development model which minimizes or even eliminates bricks and mortar and is formed around a small highly-experienced development team who design and manage the development process and clinical programs. This model has been made possible by the increasing availability of CROs and CMOs. This was not the case even 10 years ago.

ClearPath Vaccines Company (CVC) together with its partner Astellas are taking this virtual model a step further. Vaccine targets are identified, an open innovation approach is used to obtain the requisite technologies from academia or biotechs and a detailed development plan is generated by an experienced management team. A key underpinning of this model is the product development capabilities and track record of CVC's parent company, RRD International, which has experts in CMC, regulatory, quality, clinical trials and contract management. It is anticipated that funding will be provided from a variety of sources including Astellas itself, VCs, foundations and other investor groups. Each product will be developed by a separate development company of which RSV Corporation is the first example. Successful products will be acquired through options by Astellas for Phase III development and global marketing.

Dr Rino Rappuoli
Global Head of Vaccines Research
Novartis Vaccines and Diagnostics

Prediction for the next 12 months:

The vaccine industry will increasingly need to respond to and help protect populations against potential global health threats that originate in other regions. For example, the H7N9 bird flu virus began circulating in China last March, and following its emergence, Novartis helped respond to this potential public health emergency. With our partners at Synthetic Genomics Vaccines, Inc. (SGVI), we quickly synthesized vaccine viruses targeting the H7N9 virus that was found to be circulating in China and supplied synthetic genes to the US CDC in support of global public health efforts. Late last year, we announced interim results from a Phase I clinical trial with this vaccine, which showed that the majority of the subjects vaccinated achieved a protective immune response after two doses.

Last vaccination...

An adjuvanted influenza vaccine and a “TdaP” vaccine.

VIEWPOINT:
Novartis and the role of Big Pharma

How do you feel the role of big pharma is going to change in the vaccine industry in the coming year, and what are Novartis doing to ensure continuing success?

Overall, I think companies will continue to focus on new areas where there are unmet needs. For instance, we’re investing in promising earlier-stage projects such as a maternal vaccine for Group B Streptococcus (GBS), which is a leading cause of life-threatening infections such as sepsis and meningitis in newborns worldwide, as well as vaccines to help protect against hospital infections.

In terms of continuing our success, we’ll continue to focus on making our vaccines broadly available to patients around the world. Over the past year, we’ve had several noteworthy approvals, including regulatory approval of our meningitis B vaccine Bexsero® in Europe, Australia and Canada. Bexsero® is the first and only vaccine approved to help protect against MenB. I began researching a vaccine for MenB more than 20 years ago, and seeing the first doses administered to patients this past year has become a highlight of my career.

In the US, we successfully introduced Flucelvax®, which was the first seasonal influenza vaccine manufactured using cell culture technology to be approved by the FDA. Cell culture technology is the most significant advancement in flu vaccine manufacturing in more than 40 years and is an example of our continued commitment to technological advancement in vaccine research and development.

Dr Myron Levine
Grollman Distinguished Professor and Director, Center for Vaccine Development
University of Maryland

Prediction for the next 12 months:

One issue that I think worries a lot of vaccine developers is the trend for advisory committees these days to prioritize vaccine introduction, in great part, based on financial considerations, including estimates of vaccine effectiveness. One instance that's got a lot of notoriety of late is the Novartis meningococcal B vaccine. This is a difficult situation because I think everyone will have to grapple with this now, because the cost of vaccine development programs are so enormous that one has to have a certain assumption that the public health sectors, the opinion-makers and other influential groups are on the same plane as vaccine developers. If there's not a mutual assumption that a vaccine is needed and would be used, the vaccine is not going to be developed, because it doesn't take many situations like what happened in the UK deciding not to utilise the men B for there to be a very strong disincentive for vaccine developers.

Another area that I think will be quite active may be, interestingly enough, the pertussis vaccine. The acellular pertussis vaccines are just not providing the level of protection and public health impact that we need and desire. I think that this is an area where there will be a lot of rejuvenation.

Last vaccination...

The 13-valent pneumococcal conjugate.

VIEWPOINT: Vaccines in sub-Saharan Africa

What impact would a new vaccine for non-typhoidal salmonella infections have on public health in sub-Saharan Africa?

Invasive, non-typhoidal salmonella infections were serendipitously found more than 10 years ago to be a major cause of invasive bacterial disease, right up there in incidence and burden with Hib and invasive pneumococcal disease. This is in much of sub-Saharan Africa. It is not only in HIV high-prevalence areas, with HIV being one risk factor and severe anemia in malaria being another, but it's in places like Mali that have very low HIV prevalence. And the same is true of rural Gambia.

With the introduction of Hib conjugate vaccines through the GAVI Alliance, and pentavalent vaccines that contain Hib conjugate, Hib has almost disappeared in a number of countries in sub-Saharan Africa, including Mali. With the introduction of multivalent pneumococcal conjugate vaccines, once again with the GAVI Alliance subsidizing the introduction in many countries in sub-Saharan Africa, invasive pneumococcal disease is also plummeting.

The remaining major problem then is non-typhoidal salmonella. In some urban slum areas, typhoid is not uncommon, but in young children, salmonella typhimurium and salmonella enteritidis are the main serovars. The salmonella typhimurium is a very sub-Saharan-specific, unusual genetic type that is not seen in other parts of the world. There's also some preliminary data that the enteritidis strains may be special in sub-Saharan Africa. So the big question is how we control this, since we know so little about the epidemiology. For many reasons, one can argue that a vaccine to prevent invasive non-typhoidal salmonella is the way to go.

There are two groups that have candidate vaccines moving towards clinical trials. They're both quite innovative vaccines. Our group is working with industrial partner Bharat Biotech in India. The other group that is working on a vaccine is the Novartis Vaccines Institute of Global Health.

Raja Rao
Senior Program Officer, Global Health/Vaccine Delivery
Bill & Melinda Gates Foundation

How to improve public perception of vaccines:

Advocacy is the only thing that's going to improve public perception. The public is the public, and the public listens to messages. Studies aren't going to do it. It's a campaign, like an anti-smoking campaign; really showing the public the consequences. Like we used to see those black lungs or people whose jaws were cut out – these dramatic photos from tobacco use: I think it's important to really show people how nasty measles is, and I think they'll get that.

VIEWPOINT: Thermostability

What value do you see in improving the thermostability of vaccines?

One I think is, at an output level - and we have evidence strongly suggesting this – that countries can save significant resources by reducing their required financing for cold chain and reducing the required human resources in the supply chain. I think the broader thing, though, at the outcome level, is if you do have fully thermostable vaccines, or vaccines that are thermostable long enough that they go through the supply chain and remain viable, is that countries can begin to actually extend coverage. If your vaccine is thermostable, you don't need cold chain. You can extend the reach of your immunization services significantly beyond where they are today.

Do you see any promising approaches to thermostability?

There are things out there like silk proteins, sublingual gels, fast-dissolvable tablets, and certain types of lyophilized vaccines. There are some technologies today that can extend stability, like lyophilization, to the point where if you had an efficient supply chain you could claim you had a fully thermostable product.

But the issue is that there are trade-offs. So it's a question of, what are the trade-offs you're willing to make?

Will industry look more towards thermostability in the coming year?

I think the number one issue in the near-term is to take advantage of the existing thermostability of vaccines that are already approved for use. So for instance we've taken advantage of the existing thermostability of the MenAfriVac vaccine, and for that vaccine there's a pilot in Benin where that vaccine was taken out of the cold chain at the last mile. Healthcare workers and systems didn't need to make ice, they were able to outreach more effectively etcetera. PCV vaccine is stable for 30 days at higher ambient temperatures, and so relabeling those vaccines to reflect their true thermostability, looking at the data, doing the required studies, I think that's a 'no regret' move that can happen and is happening over the next 12 months.

Dr Stephen Albert Johnston
Co-Direct, Center for Innovations in Medicine, Biodesign Institute
Arizona State University

How to improve public perception of vaccines:

I think there are a lot of people out there doing a good job in terms of public education and combating misinformation. Other than that, which is hard slogging, the thing that might change the opinion enough is if some vaccine came along which everybody would want. You can get away with not taking these vaccines because of herd immunity and we've got rid of most things. But let's say we develop a prophylactic cancer vaccine. Well, there's no herd immunity there, and then I think everybody will want it! So I think that would change people's opinions very quickly.

Last vaccination...

The yearly flu vaccine.

VIEWPOINT: Immunosignatures

How does the immunosignature tool work?

It is taking the antibody diversity which is there in a person and then putting that diversity up against a diversity of peptides, and then pulling those two apart and seeing what's on the surface. It gives a fingerprint, a signature, of what the antibody profile was. It's not surprising that the antibodies are sensitive to your health status, and I think people will generally buy that idea. It's more sensitive than I thought. But the interesting part was what it takes to read out that diversity. There the trick was to, in a way, splay out the antibody diversity sensitively so you could see it. That was the trick.

How could this be applied to vaccines?

We're not positive yet, but so far the work that we've done, both ourselves and in collaboration with others, looks like it can hopefully be able to tell you how your vaccine is responding with higher dimensions. The idea is that you give a vaccine and then you do this extensive analysis of cytokines and T- and B-cells and you composite that together to create a profile of your vaccine. Then you can compare two vaccines and see what's good and what isn't. What we've found is it looks like the B-cells themselves, the antibodies they produce, are producing about as much information as that extensive work-up of your immune system is. In the paper we published, we showed that we could, in a model system, effectively apply the same sort of ideas as systems vaccinology but just from one-tenth of a drop of blood, diluted and put on these chips. We think it has a lot of possibilities there.

Another part of our group is trying to work on a prophylactic cancer vaccine, and it actually looks relatively promising but the biggest problem people seem to be pointing out now is not that it couldn't be done but it could never be validated, because it would take too long and cost too much. What we're looking for is to use this as a way of detecting cancer very early so we could shorten a clinical trial of a prospective preventative cancer vaccine. We've been pushing on that quite a bit. Instead of waiting 10 years, you might be able to conduct a trial in three.

Devi Thomas
Director, Shot@Life
United Nations Foundation

What do you think is needed to improve the collaboration between industry and non-profits?

Shot@Life is very lucky to work with corporate partners, and we work closely with Walgreens, diapers.com (which is part of the Quidsi family of companies), and Johnson and Johnson. These partners are all helping to amplify the message for us. Whether that's through creative cause-marketing campaigns and fundraising, or whether it's by getting people to share information about global vaccines, it's an incredibly important voice and certainly the type of reach that we would not be able to effectively get to if we did not have that kind of partnership.

Last vaccination...

I received the flu shot at Walgreens, as part of their "Get a shot, give a shot" campaign.

VIEWPOINT:
Preventing disease in developing countries

What is Shot@Life?

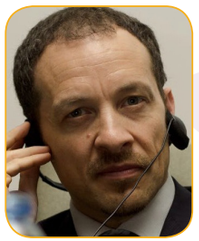
Shot@Life is a campaign that helps bring Americans closer to the great work that the United Nations and GAVI are doing to prevent disease in developing countries. The primary way that Shot@Life does this is to share the message that every 20 seconds a child is dying from a vaccine-preventable disease. By sharing this message, we are asking Americans to get involved. We do this by asking them to donate to help us to provide vaccines to the developing world and to children who desperately need them. We're also doing this by asking Americans to advocate for the issue, such as to go to US policy makers and their members of Congress, and to talk about why it's important to continue to support organizations like the UN and like GAVI in the work that they're doing to prevent childhood deaths.

Could you tell us a bit more about social marketing and what that means?

Shot@Life, like many of the social marketing campaigns you see out there, really uses messages, multimedia, the power of social media, the power of partners like corporate partners, or organizational partners like the American Academy of Paediatrics, or just incredibly active social groups, to get the message out there and get more and more Americans involved. We have a constituency of 200,000 and we started from scratch in April 2012. Among that constituency, we have 581 active Shot@Life champions.

Have you seen successes so far with the campaign?

Absolutely. As a campaign, we have been able to send several advocacy messages through to members of Congress. In the upwards of around 18,000-20,000 advocacy actions have been taken by the campaign. We've also been able to raise significant funds, upward of $1 million, to be able to actually deliver vaccines to children in need. We've had a significant amount of luck in building our champions throughout the country so we're now in 49 states, which is really a significant boost considering we started with a small group of 100 champions in 2012.



Stefano Malvolti
Director, Vaccine Implementation
GAVI Alliance Secretariat

Prediction for the next 12 months:

There is a need for new presentations of vaccines that are more tailored to patient needs. If you have a vaccine that is thermostable for a long period of time, if you have a vaccine that instead of requiring a three-dose schedule requires a one-dose schedule, if you have a vaccine that can be delivered needleless: all these type of innovations, that have been very much neglected so far, would completely change the space of immunization in both the developing and developed world.

One space, of course, is the development of vaccines against diseases for which we don't have vaccines today; malaria, tuberculosis – having a new generation of TB vaccines – and HIV. We have a malaria vaccine in the pipeline, and it may become available in the next few years. Then also looking at vaccines for new emerging diseases like dengue.

Lastly, there is the space of cancer vaccines, which is very fascinating and interesting.

Last vaccination...

Influenza, right before Christmas.

VIEWPOINT:
Supply Chain challenges

What elements of the supply chain are most challenging today and how could they be solved?

There are multiple aspects – it depends what you mean by supply chain. Traditionally in the vaccine space, supply chain has been very much identified with the cold chain. Indeed, the cold chain does have some substantial challenges.

Another major area of concern that is emerging more and more, in particular where resources become more and more scarce (financial resources from donors as well as from national government) is stock management. Some countries have some control or basic way of managing stock – some have a reasonable one, some others don't.

The focus is, can we have the right vaccine, at the right place, at the right time? This seems to be very basic, but the right vaccine being an effective and functioning vaccine, which has not been damaged throughout transportation by temperature or other mishandling, at the right place, where the patient shows up, isn't that simple.

Dr Lenny Moise
Director of Vaccine Research
EpiVax Inc

Prediction for the next 12 months:

I think that the importance of the human microbiome is going to emerge as an important factor in vaccine design as well as vaccine testing. Different populations respond differently to the same vaccine, and it is now thought that the microbiome is one of the factors that can influence that. Genetics, socioeconomic conditions, nutritional status, and a number of other factors can contribute to it, but I think that a greater awareness of the importance of the microbiome on human immune development and homeostasis will lead vaccine developers to consider its impact on how humans respond to vaccines.

Last vaccination...

The trivalent inactivated influenza vaccine this season.

VIEWPOINT: Incorporating informatics and genomics

How can informatics and genomics improve vaccine design?

Informatics and genomics are means of designing vaccines in a rational way to carefully select the antigens that are built into a vaccine, to define the minimal essential information needed to generate protective immunity. It is not the time-honored 'isolate, inactivate and inject' approach. Informatics and genomics are the basis of reverse vaccinology. We're thinking more about what a vaccine should contain. We have the tools – informatics and genomics, as well as new knowledge of immunology and 'omics technologies such as, proteomics and transcriptomics, that provide additional information to rationally select antigens.

What's the need for reverse vaccinology?

For many pathogens that have no licensed vaccines today, inactivated or live-attenuated vaccines may have too much information; we don't know exactly what is in them and that may explain why these strategies have not progressed. In a sense, we have a smarter way of producing a vaccine by tearing down the pathogen and then rebuilding it in a form that will get across what is essential to generating protective immunity. Reverse vaccinology is not about what we take out of a pathogen to create a vaccine; it's what we build from the ground up - critical antigens identified using computational and experimental techniques and best-in-class delivery vehicles and adjuvants.

Reverse vaccinology also affords the opportunity to think about how antigens may cross-react with sequences that are homologous to commensal or pathogens that a person has been exposed to in the past. We now have computational tools available to consider and predict potential cross-reactivities which could lead to muted, or worse yet detrimental, immune responses. With the ability to more carefully select antigens for vaccines by taking potential cross-reactivities into account, it's now possible to focus in on pathogen-specific sequences like never before.

Louis Cantolupo
Director of Business Development
Valneva

How to improve public perception of vaccines:

I think at a fundamental level, the dangers of not being vaccinated are poorly appreciated. It might be that to get people to vaccinate is going to result more from a primary decision making process. It could come along the lines of peer pressure. So in an area where you have influenza, chicken pox, mumps, rubella and other diseases of this ilk, these are mostly survivable, so choosing not to vaccinate because these diseases are survivable sadly becomes a privileged position, like buying a television. It's the classic first world problem.

With such decisions we are influenced by our peers. Usually when you buy these things your peers will say "Why would you pick that one?" If it came from your peers, people you trust, your friends, your co-workers, your family – "Why did you not vaccinate?" – it puts a little bit of pressure on them.

Last vaccination...

Influenza. The last non-flu vaccine was for yellow fever.

VIEWPOINT:
New opportunities for vaccines

How do you see things changing in the next 12 months?

For cell platforms in the next 12 months there will be new market opportunities, not just different types of vaccine but actual real physical markets, and in particular the BRIC regions. Across the industry, you're going to see with cell-based technologies more spread into new geographies.

Two things have had me curious over the last three or four years. We see in at least oncology and inflammatory diseases, rare disease indications – these orphan-type status monikers that were given to these indications that have a very small population. Some product development seems to happen really fast, and a lot of it can be due to it being a small population that you're treating so it's a little more clear cut in terms of a defined endpoint, especially when other treatment options are limited to non-existent. At the same time, it can be hard because you have to find the patients. But they seem to be able to rapidly develop these products and they're very successful. So it's not only a rapid product development cycle but it's also very successful. With these rare disease indications, their profit opportunity is very high and so that's part of the incentive. With vaccines it's very difficult to do that because it's mostly for public health etcetera, but what can we learn from the orphan drug developers and apply it to infectious disease - in particular in product development? What are they doing on the product development side that could be transferable over into vaccine development?

I think new technologies, or the repositioning of new technologies, is going to become more prominent. You see a lot about massively parallel sequencing not only being used to test for product quality but also for the discovery of new epitopes and testing for antigenic variability – in particular in pathogens like influenza and HIV. I think we're going to see a lot more of MPS being used, not only in testing product quality but also in discovery.

Dr Marc Mansour
Chief Operating Officer and Director
Immunovaccine, Inc

Prediction for the next 12 months:

I think we're on the cusp of some very dramatic things happening with cancer vaccines. The first step is everybody in pharma recognizing that cancer vaccines are not a bad thing and they can be useful. I've heard comments from some of the major pharmas that we need to throw away all our biases towards cancer vaccines and rethink about what makes sense to combine with our compounds, what are the right targets to go after, what's the right vaccine design, what kind of clinical data is there to the mechanism of action of these vaccines to give us confidence that we should jump in and try them. We shouldn't just assume they're not going to work. They've been used the wrong way, they didn't have any data to support that they had a chance to work, etcetera.

I think they're starting to change. You're seeing companies in early stage doing combination trials now with the combination of two vaccines, for example. I think right now, with the momentum in immune therapy and the realization that checkpoint inhibitors are probably going to be most effective if they're combined with a cancer vaccine approach, even if work by the likes of GSK failed, I don't think the cancer vaccine industry is going to be set back so far.

Last vaccination...

Influenza.

VIEWPOINT:
Combination therapies

What's the need for combination therapies and how much of an improvement can we see compared to individual vaccines?

I think there's recognition now in the research community, and in pharma, that cancer vaccines are now not likely to work very well for a number of reasons. First of all, in most cases you're trying to raise an immune response against a self-antigen, so it's very difficult to do that. Of course, adjuvant technologies might help break tolerance, but it's still going to be difficult. So if you can modulate the immune system so that it becomes more receptive to vaccination and gives the vaccine a boost to generate a stronger immune response, people are going to try and do that. It makes perfect sense that you would try to do that if there are compounds that you could use safely and efficiently with vaccines. We refuse to do a trial with cancer vaccines as a monotherapy, period. We will always combine it with something.

What's more exciting than that basic approach is to combine cancer vaccines with some of the hot immunotherapies that are out there, especially checkpoint inhibitors. What everybody's excited about now in immunotherapy is anti-PD-1 and anti-CTLA-4. BMS, Merck and Roche are all driving these checkpoint inhibitor programs, and what these monoclonal antibodies are good at is activating T-cells in a blanket, general way. What the pharmas are moving towards now is combining their checkpoint inhibitors with targeted T-cell activation therapies – and that's vaccines.

Dr Maria Elena Bottazzi
Director Product Development
Sabin Vaccine Institute

Prediction for the next 12 months:

Novel and innovative models to decrease this 1/99 gap (as explained to the right) in Vaccine R&D funding especially for NTDs will be essential.

The business model utilized by Product Development Partnerships (PDPs) will continue to thrive. PDPs are now diversifying their funding portfolios and they are creating new and novel strategic alliances, especially with small and medium enterprises, to attempt to advance and even accelerate development of new vaccines. PDPs continue to be the promise for the new and next generation of vaccines that will have a huge global health impact.

Last vaccination...

Flu vaccine.

VIEWPOINT:
Collaboration between industry and non-profits

What do you feel is needed for collaboration between industry and non-profits to improve, and what impact would this have on vaccine development and delivery?

Collaborations between industry and non-profits would benefit with an increase of providing better access to new technologies and discoveries such as in the area of adjuvants and novel delivery platforms. Of particular importance would be how industry could be an influencer or an accelerator especially in the space of global health vaccine R&D.

As stated in the recent G-FINDER (Global Funding of Innovation for Neglected Diseases) Report, worldwide only approximately $3 billion is spent annually on global health research for diseases disproportionately affecting poor countries. However most of the funds go towards the big three diseases (HIV/AIDS, malaria and TB). Support for the neglected tropical diseases or ‘NTDs’, such as hookworm infection, ascariasis, trichuriasis, schistosomiasis, onchocerciasis, dengue fever, Chagas disease, and leishmaniasis continues to lag behind.

Dr John A. Howard
President
Applied Biotechnology Institute

Prediction for the next 12 months:

While the vaccine industry has been playing a role in public healthcare for many years and has had one of the greatest impacts on human health, the next 12 months should bring the industry great progress in vaccine development and expand the boundaries of research into new targets, treatments and indications.

From the research community, our understanding of the immune system and its interaction with disease has increased significantly. We will see more impact from therapeutic vaccines, in areas from cancer to smoking cessation and addiction.

In addition, advancement of new vaccine technologies, manufacturing and expression systems are bringing innovation and new methods for producing these vaccines to provide an even greater impact on vaccine effectiveness, access and ultimately maintaining health.

From the medical community, we will see a greater emphasis on the importance of immunization, not just for children but also throughout an individual's life. A greater awareness and understanding that vaccines have a place in maintaining health through the spectrum of one's life will be the focus.

Last vaccination...

I receive a flu vaccine every year.

VIEWPOINT:
Hepatitis B Vaccines

How will perfecting the thermostability of a hep B vaccine impact on the wider industry?

Perfecting thermostability for vaccines could have a very broad impact on reliability of the vaccine supply and provide greater access to many life-saving vaccines. Eliminating cold chain requirements and increasing the ability to stockpile vaccines at most any location would provide great benefits to the industry, particularly in the developing world.

An additional benefit of the system we have developed at ABI for vaccines is enabling oral delivery. An oral version may increase compliance and greatly reduce costs of administration, especially in remote locations, by eliminating the need for needles, trained medical staff to give the injection, and additional visits to a medical facility for booster shots. The demonstration of the technology with a hepatitis B vaccine encourages the development of other oral vaccines. This would be another very big impact on the broader industry.

Dr Richard A. Insel
Chief Scientific Officer
JDRF

Prediction for the next 12 months:

There will be increasing interest and activity in cancer vaccines and vaccines for autoimmune diseases.

There are some concerns among the general public about the safety and risk of vaccines. In my opinion, to improve public perception in the future, stakeholders need to better communicate the benefits and risks of vaccines.

Last vaccination...

Influenza vaccine.

VIEWPOINT:
Diabetes vaccines

How could a vaccine for type-1 diabetes replace insulin injections, both preventatively and for those already diagnosed?

Vaccines are currently being developed for both the prevention of symptomatic type 1 diabetes (T1D) and for conferring immunoregulation in new-onset type 1 diabetes. Multiple different vaccine formulations are being developed.

In the USA and Europe today, children from the general population and relatives of individuals with T1D are being screened for risk and are being recruited into vaccine trials for either prevention of the pancreatic beta cell autoimmunity associated with T1D or for regulation of ongoing autoimmunity prior to symptomatic disease.

In new-onset T1D, vaccines are being applied to regulate autoimmunity to preserve residual beta cell function, which is usually present at the time of diagnosis, to improve glucose control and decrease insulin dose requirements. The long-term goal will be to combine diabetes vaccines with other therapies to restore insulin independence in both new-onset and established T1D.

Anthony Ford-Hutchinson
Independent Consultant

Prediction for the next 12 months:

Perhaps the biggest excitement in oncology has been the clinical data obtained with the checkpoint inhibitors, in particular anti-PD1 and anti-PDL1 monoclonal antibodies. These results suggest that cell-mediated immune responses can have significant effects on patient survival in difficult to treat tumor types. First generation cancer vaccines have had either no or modest benefits in oncology patients. One interpretation of this is that these vaccines raised very few cells capable of killing tumors. However, the CAR-T technology developed at the University of Pennsylvania has shown that it is possible to re-program immune T-cells to effectively kill cancer cells. This is an individualized approach that will be difficult to roll out on a large scale. The question now is whether newer technologies, such as either viral vectors or immuno-enhanced DNA electroporation, will provide enough “kick” to eliminate tumor cells and whether the efficacy of such cancer vaccines can be enhanced by co-administration of immunomodulatory molecules, such as anti-PD1 antibodies.

Last vaccination...

Seasonal flu (high dose)

VIEWPOINT:
Technology innovation and viral diseases

What innovative technologies have the most potential to address unmet needs for vaccines for viral diseases?

With regard to viral diseases, there are unmet needs for both therapeutic and prophylactic vaccines. For therapy, the need is to produce powerful cell-mediated immune responses. The most effective approaches to this use either in vivo electroporation of DNA, allowing for the co-administration of antigens and cytokines, or the use of viral vectors using a prime-boost strategy. An example of the latter would be the use of chimpanzee adenovirus vectors as priming agents followed by the use of Modified Vaccinia Ankara (MVA) as boost.

Two of the diseases that are most likely to benefit from these types of approaches are pre-malignant HPV infections and chronic hepatitis B infections. With regard to HPV infections, Inovio, the lead exploiter of DNA electroporation, has completed enrollment on a Phase II study, the results of which should become available in 2014. For the treatment of hepatitis B infections, it will probably be necessary to use approaches such as those pioneered by Inovio and Okairos, in combination with multi-drug therapy to bring down the viral load and possibly immunotherapeutics, such as anti-PD1 antibodies.

With regard to preventative vaccines for viral diseases, perhaps the biggest unmet needs are for vaccines to prevent dengue fever and RSV infection. For dengue fever, the challenge has been to produce a vaccine that will produce antibodies to, and hence prevent infection with, all four serotypes simultaneously. For RSV the challenge is that the population most in need are young infants where the presence of maternal antibodies is a significant barrier to vaccination. The most favored route is the intranasal route, which is complicated by the fact that young babies are obligate nose breathers.

Marie Mazur
Global Head, Influenza
bioCSL

Prediction for the next 12 months:

It is likely that we will continue to see companies enter and exit the vaccine and influenza markets due to challenges of manufacturing, changes in strategy and commercial or compliance factors. From an influenza vaccine perspective, we anticipate some unique vaccine delivery options may become available and the possibility of a US adjuvanted influenza vaccine. One also expects continued advancement in the scientific knowledge of potential pandemic strains, possibly as a result of clinical efficacy studies within naïve populations. Through these efforts we can expect a better understanding of immune correlates of protection.

Last vaccination...

The 2013-2014 Influenza Vaccine!

VIEWPOINT:
Seasonal and universal flu vaccines

What progress have you seen in the development of both seasonal and universal flu vaccines?

We have seen the maturation of seasonal influenza vaccines which have evolved from monovalent to trivalent (TIV) and more recently quadrivalent (QIV) formulations. Although public health policies have been steadily progressing towards universal influenza immunization, vaccination uptake within specific groups remains insufficient and well below the World Health Organization's objective of 80-90%. Additionally, much needs to be done to enhance the availability of influenza vaccination within lower-income countries.

TIV injectable vaccines remain the dominant vaccine within the market. The first differentiated vaccine was the live-attenuated TIV vaccine, administered via intranasal route. Large vaccine suppliers have invested in strategies to provide products with better efficacy to the elderly: a high-dose US vaccine and an adjuvanted European vaccine are now licensed, but still only represent a small percentage of products utilized. More recently, recombinant and cell-culture produced vaccines have entered the market, though well differentiated benefits remain to be recognized by providers. Finally, in the area of vaccine delivery, many startup biotech companies have focused their efforts on developing new modes of vaccine administration with some examples of commercial success.

Regarding the future and pandemic influenza, experience gained from the 2009 pandemic vaccination program has stimulated funding for new technologies targeting acceleration of vaccine production and increase of production volumes. Alternate potency assays and sterility testing and implementation of some of these technologies are promising, although the realization of these technologies will require demonstrated human safety and efficacy, a time-consuming and resource-demanding requirement.

Influenza vaccines are different from all other vaccines; they require a new annual formulation almost every winter. Universal approaches that target highly-conserved regions or internal proteins through CD8 T-cell responses hold promise, yet are still in the development phase. Difficulties in evoking specific immune responses to these regions without molecular evolution, whilst ensuring vaccine safety, are still significant hurdles.

Dr Noni MacDonald
Professor of Paediatrics
Dalhousie University

Prediction for the next 12 months:

We're going to have some new anti-vaccine complaints, because they come every year.

Also, I think there's going to be more attention paid to vaccine hesitancy. The WHO working group on vaccine hesitancy will have its report out probably by the late fall and a number of countries have put together vaccine hesitancy committees to try to address this in a better way.

There are a number of studies and polls that have been done to show that if it's a very old vaccine that has been around for a long time, people are usually much less hesitant about it. But if it's a new vaccine, or a vaccine that's new to that particular population or community, or it is being used in a different way, then people are much more hesitant. We just need to understand that, accept that and think about how to deal with that positively.

Last vaccination...

Flu vaccine in the fall, as I have done every year since 1976.

VIEWPOINT: The anti-vaccine movement

What impact can scientific vaccine professionals have on the anti-vaccine movement and parental decision-making?

The anti-vaccine movement per se is very hard to influence. What healthcare providers need to do is influence parental decisions and individual decisions about getting immunized. We do know anti-vaccine websites influence vaccine choice and your decision-making, and we also know that the most important factor in making the decision is what your healthcare provider tells you to do. We need to be influencing healthcare providers to do this in the best way, to positively influence parents in making their decisions; how you frame what you say makes a difference.

Something else we do know is that stories are incredibly powerful. Anti-vaccine websites use that all the time. They don't use evidence, they use stories. There are two kinds of stories we need to tell. We need to have parents tell what happens when their child is not immunized, and we also need to tell the story of "well look, a million kids got immunized here and none of them got this disease".

So we haven't framed what we say very well. We haven't used the right kind of language. We have consistently pummeled people with evidence, but evidence doesn't change your beliefs – and beliefs are what drive your decision-making.

The anti-vaccine lobby itself is extraordinarily hard to change, because they are convinced of their beliefs. Even though you point out to them the irrationality, the lack of evidence, and the lack of logic – it still doesn't change them.

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