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Food and Drug Administration

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1. Hurdle Identification. Please describe the product development issue, the nature of the evaluation tool that is out-of-date or absent, how this problem hinders product development, and how a solution would improve the product development process. Please be as specific as possible.

1 Hurdle: There is no system set up for advocacy groups to interact with FDA and others on these issues.

2 Hurdle: The clinical trials system needs big improvement. There is no national system for clinical trials that is fully integrated and links all the trials, people, and results and science together, additionally there is no system for diseases like pancreas cancer that is modified to fit the needs of the disease and the community. There is no national pancreas biospecimen system or patient registry system to accommodate research.

3 Hurdle: Clinical trials design and what it takes to get drugs and treatments approved is an obstacle. The current system of how we do clinical trials is too slow, it takes way too long to get drugs to be tested empirically. The clinical trials system and product development is currently a one size fits all system. This does not work for diseases like pancreas cancer where the mortality rate is so high and so fast and the overall patient community is small in patient numbers.

4 Hurdle: The science is not being well managed and mapped.

#5 Hurdle: System is not set up for emerging science i.e. molecular based treatments and tailored treatment based on a patient's genetic blueprint. Assays for diagnosis, choosing treatments, looking at response to treatment etc. do not exist for pancreatic cancer. Imaging is another area that is in great need for diagnostics and treatment management.

2. Please rank each hurdle identified in Question 1, above, in priority order according to which hurdles create the most severe product development problems. That is, which problems present the greatest opportunity for improving product development processes? Our goal is to identify those aspects of product development that would most benefit from new evaluation tools.

These are all very important, however in order for some to happen, others need to happen first. So they are more in order of chronology than priority.

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2 Hurdle: The clinical trials system needs big improvement. There is no national system for clinical trials that is fully integrated and links all the trials, people, and results and science together, additionally there is no system for diseases like pancreas cancer that is modified to fit the needs of the disease and the community. There is no national pancreas biospecimen system or patient registry system to accommodate research.

3 Hurdle: Clinical trials design and what it takes to get drugs and treatments approved is an obstacle. The current system of how we do clinical trials is too slow, it takes way too long to get drugs to be tested empirically. The clinical trials system and product development is currently a one size fits all system. This does not work for diseases like pancreas cancer where the mortality rate is so high and so fast and the overall patient community is small in patient numbers.

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3. For each problem identified, please indicate the type of drug, biologic, or device to which the hurdle applies.

Our answer: This applies to any and all drugs for pancreatic cancer, imaging of pancreatic cancer for detection and diagnosis and monitoring of the effects of treatment. This includes treatment and symptom management and overall management of the disease. Prevention of pancreatic cancer is on the distant horizon, but we need to first be able to diagnose it at the earliest possible time to maximize the effects of treatment and interventions.

4. For each problem identified, if a solution would facilitate the development of drugs, biologics, and/or devices for a particular disease or categories of disease, please indicate which diseases would be affected?

PANCREATIC CANCER and other cancers as well that are under researched and progress has been virtually non existent.

5. Nature of the Solution. For each problem identified, please describe the evaluation tool that would solve the problem and the work necessary to create and implement the tool/solution. For example, would a solution come from scientific research to develop a new assay or validate a new endpoint? If the solution involves biomedical research, please specify the necessary research project or program. Would a tool be developed through data mining or computer modeling? Would the right tool be a new FDA guidance or industry standard? If work on a solution is underway, what steps remain? Are there other innovative solutions that could be explored?

1 Hurdle Solution:

- a) Develop a working partnership with key advocacy groups and key stakeholders to develop a national plan. Bring together experts in pancreatic cancer and develop a national game plan to get develop novel and innovative ideas that can be validated, approved for use in patients.
- b) Plan that is flexible, not bureaucratic and cumbersome, allows collaborative and progressive actions to be taken. Don't get bogged down in politics and policy, but one that has the scientific freedom, ability to change regulations if warranted, while protecting safety and rights of patients.
- c) Identify barriers to drug development on disease by disease basis, cross map them to determine similarities and differences, then map the national strategy taking these elements into account.

2 Hurdle Solution:

- a) Create a network (can be virtual) and coordinated system that can translate biological insights into clinical use and translate clinical observations into laboratory investigations.
- b) Utilize information technology, to develop an appropriately integrated system that will serve as an infrastructure to build a national research system that includes clinical trials system.
- c) Develop a coordinated system especially for cancers like pancreas cancer. The PanCAN Research MAP and PanCAN Clinical Trials database will begin

to create the information base we need to get the job done.

- d) Develop key infrastructure resources such as biospecimen network and patient registry that contains clinically annotated and relevant data.
- e) Develop business plan and execute the plan with key stakeholders at the table.
- f) Develop clinical trials model systems that are novel and not duplicates or minor revisions of old systems that do not work for pancreas cancer.
- g) Develop financial and academic career model for researchers and industry in under researched diseases.
- h) Develop everyday methods that enable and empower the patient to be involved in either or both, specimen donation and clinical research including developing a national "ATM" type system for integrating clinically annotated data that will be coded to the patient specimen, to a national patient registry system as well as to the patients own medical records.
- i) Develop a system that analyzes drug failure and work to improve the rate of failure in pancreatic cancer that is disproportionately high.

3 Hurdle Solution: A system that is faster and more flexible in pancreatic cancer. Optimize novel clinical trials specific to pancreatic cancer, do multi drug and combination trials in more of a "plug and play" type mindset.

- a) ways to get patients into clinical trials sooner and more patients onto trials
- b) ways for the advocacy community to work with the research community and FDA and NCI
- c) develop the appropriate standardized technology and platforms for standardized protocols for specimen handling and acquisition.
- d) integrate other disciplines that are essential to the process but may not be involved in oncology, such as gastroenterologists, general surgeons, primary care physicians, basic scientists, epidemiologists etc.
- e) explore alternative trial designs to address specific problems in pancreatic cancer for example: the difficulty of assessing response or benefit in patients with locally advanced and metastatic pancreatic cancer and the activity of new therapeutic strategies that may not kill tumor cells, but stop their growth.
- f) validate novel surrogate endpoints, including disease stabilization, biochemical markers, and results of functioning imaging studies.
- g) design studies to include correlative components and design studies to maximize and leverage the amount of scientific data that is captured.

- h) develop system for better sharing of data, mining and statistical, and mathematical models.
- i) develop standardized tiered consent form
- j) Use scientific tools to select patients for trials and treatments based on algorithm that optimizes potential utility of treatment.

4 Hurdle Solution:

- a) Create mechanisms that get key stakeholders working well together.
- b) Using the PanCAN-NCI Pancreatic Cancer Research MAP, and PanCAN's proprietary clinical trials database, work together in understanding the clinical trials landscape and the state of the science in pancreas cancer.
- c) Work closely with FDA, NCI and their clinical trials experts along with the experts in pancreatic cancer clinical trials. There should be a national plan for clinical trials development that is cross coordinated within the public and private sectors.
- d) Facilitate the discovery and development of targeted therapeutics by using a national plan based on the PanC Research MAP.
- e) Communicate the science, the opportunity and the results to the patient community and this can be accomplished through working partnerships with the pancreatic cancer advocacy community.
- f) Develop mechanisms to ensure that research results and treatment advances are integrated out into community settings.

#5 Hurdle Solution:

- a) Provide incentives to industry and equipment manufacturers to work with the research community in understudied diseases and diseases with high mortality rates that have little to no measurable progress in the last ten years.
- b) Facilitate interactions and collaborations between Key Advocacy groups , FDA, Industry, and NCI programs such as the Specialized Programs of Research Excellence (SPORES), Early Detection Research Network (EDRN) and the Mouse Models of Human Cancer Consortium (MMHCC), the Pancreatic Cancer Genetic Consortium (PacGene) and the Pancreatic Cancer Collaborative Registry (PCCR).
- c) Identify the problem areas and the opportunities for scientific advancement.
- d) Develop simple, reliable, and valid instruments for assessing clinical benefit in pancreatic cancer patients.

e) Develop an open source national pancreas cancer biospecimen repository system and patient registry as described in the National Biospecimen Network Blueprint.

f) Develop everyday methods that enable and empower the patient community to be involved in either or both, specimen donation and clinical research this includes developing a national 'ATM' type system for integrating the clinically annotated data that will be coded to the patient specimen, to a national patient registry as well as to the patients own medical records.

6. For each solution identified, please indicate which could be accomplished quickly, in less than 24 months, and which require a long-term approach?

If you bring together the right people with the right mindset and the right attitude. Every one of these solutions could be integrated into a pilot program that could be up and running within 24-36 months and validated within five years. This would require adequate resources and the will of many, but it is possible. In order to accomplish this, it needs to be a committee infrastructure and process that is not totally managed and run by any government agency.

We can accomplish this by developing a pilot program that brings in business expertise from the private sectors, advocacy sectors, information technology sectors and other key private sector groups that have experience in designing nationally integrated systems. The government agencies while key stakeholders, their most important role is to bridge and link together innovative science with policy.

1 Hurdle: There is no system set up for advocacy groups to interact for the purpose of action with FDA and others on these issues.

Time Frame for Solution: This could be up and running within 12 months.

2 Hurdle: The clinical trials system needs big improvement. There is no national system for clinical trials that is fully integrated and links all the trials, people, and results and science together, additionally there is no system for diseases like pancreas cancer that is modified to fit the needs of the disease and the community. There is no national pancreas cancer biospecimen system or patient registry system to accommodate research. The amount of support for the infrastructure and running of publicly funded clinical trials is inadequate.

Time Frame for Solution: This can be accomplished in 24 months. With key milestones in place at earlier intervals. Pilot could be up and running within 24 months.

3 Hurdle: Clinical trials design and what it takes to get drugs and treatments approved is an obstacle. The current system of how we do clinical trials is too slow it takes way too long to get drugs to be tested empirically. The clinical trials

system and product development is currently a one size fits all system. This does not work for diseases like pancreas cancer where the mortality rate is so high and so fast and the overall patient community is small in patient numbers.

Time frame for solution: A pilot system can be developed within 24 months if developed in conjunction with previous steps required for a national system.

4 Hurdle: The science is not being well managed and mapped.

Time frame for Solution: Can be executed in the concurrent 24-36 months along with the previous recommendations.

#5 Hurdle: System is not set up for emerging science i.e. molecular based treatments and tailored treatment based on a patient's genetic blueprint. Assays for diagnosis, choosing treatments, looking at response to treatment etc. do not exist for pancreatic cancer. Imaging is another area that is in great need for diagnostics and treatment management.

Time frame for Solution: This would be integrated into a pilot program and could be up and running in 24-36 months.

7. For each problem identified, what role should FDA play and what role should be played by others? Should FDA play a convening role, bringing the relevant parties together to discuss an approach or solution? If so, who else should participate? Should FDA coordinate scientific research, the results of which would be publicly available? We are seeking input on ways to target FDA scientific and collaborative activities to help industry bring more safe and effective medical products to us for review.

Most of our perspective is addressed in previous solutions to the hurdles. The government agencies such as FDA are key stakeholders, and their most important role is to bridge and link together innovative science with policy. To help address the barriers whether they are real or perceived and then work with the community to address each barrier through re-engineering and re-tooling of the system. The Critical Path Initiative is a very good first step. FDA's role is to be part of the solution and to be a team player. FDA can assist in facilitating collaborations. FDA can help meld science and innovative thinking as it relates to policy modifications that might be required to pilot innovative solutions to age-old problems. FDA can take the lead and demonstrate the capability and expertise of the FDA in drug development for cancers like pancreatic cancer that have suffered from a tremendous lack of progress. FDA can bring all of us together so we can collectively figure out a way for organizations to work together in a bureaucratic situation. FDA's role is to be dynamically responsive in working with the community to develop the most effective and efficient way to

safely expedite innovative drugs and treatments to patients.

8. What factors should guide FDA in setting priorities among the hurdles and solutions identified?

Cancers that have little or no treatment options available should be given the highest of priorities. One key factor needs to be a complete and thorough examination of public and private efforts aimed at disease specific cancer research and the research progress for each area. MAP out all approved treatments including compendia listings. Drug development is a disease specific endeavor and needs to be reviewed on that basis. Cross map the progress with the state of the science to determine scientific areas for opportunity that take advantage of technology. Upon completion of that exercise, the FDA needs to look at mortality of cancers and which cancers have not enjoyed any progress in treatment, diagnosis and management. There should be a high priority given to the needs of cancers like pancreatic cancer, the 4th leading cause of cancer death and one which the patient community suffers from a severe lack of treatment options. In cancers with many treatment options, FDA should review areas of need and gaps in managing those types of diseases and then facilitate collaborations aimed at national strategies for those cancers.

Thank you very much for the opportunity to offer comment. We have attempted to scratch the surface on some very important issues for the entire community and look forward to engaging with you on more substantive and progressive interactions. The newly created Office for Oncology Products will hopefully help us all move in the direction needed.

We are ready when you are to get started, we have an entire patient community of pancreatic cancer patients and families that is counting on all of us.

Respectfully,

Paula Kim

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Co-founder