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INTERVJU INTERVIEW

# Ljudi iza Philip Morris nauke
# **Intervju sa Blejnom Filipsom**
# The People behind Philip Morris Science
# **Interview with Blaine Phillips**

**Blaine Phillips**

Toksikološka procena ima za cilj da potvrdi da li smanjeno stvaranje štetnih i potencijalno štetnih sastojaka, na primer, dovodi do smanjene toksičnosti i smanjenog rizika od razvoja bolesti povezanih sa pušenjem u laboratorijskim modelima. U pretkliničkoj naučnoj i toksikološkoj proceni, naučnici *Philip Morris International* (*PMI*) iz različitih oblasti biologije, farmakologije, toksikologije, nauke o aerosolu, biostatistike i računarskog modelovanja, posvećuju svoje vreme pretkliničkoj naučnoj proceni svih PMI bezdimnih proizvoda. U intervjuu sa Blejnom Filipsom, generalnim direktorom u PMI istraživačkim laboratorijama u Singapuru, biće predstavljena procena aerosola bezdimnih alternativa na različitim životinjskim modelima bolesti, u poređenju sa dimom cigareta.

Toxicological assessment aims to confirm whether the reduced formation of Harmful and Potentially Harmful Constituents (HPHCs), for example, leads to reduced toxicity and reduced risk of smoking-related diseases in laboratory models. In Preclinical Science and Toxicology, *Philip Morris international's* (*PMI*'s) scientists from various areas of biology, pharmacology, toxicology, aerosol science, biostatistics, and computational modeling, dedicate their time to preclinical scientific assessment of all PMI's smoke-free products. In an interview with Blaine Phillips, General Manager at the Philip Morris International's Research Laboratories in Singapore, will be presented the assessment of aerosols of smoke-free alternatives in various animal models of disease, compared to cigarette smoke.

**1. Kao naučnik koji radi za privredu, kako izgleda to kada je poslovni model zasnovan na dostignućima Vašeg istraživačkog tima? I da li očekujete da i drugi biznisi razmišljaju u tom pravcu?**

Većina naučnika dolazi iz akademskog okruženja, koji napreduju kroz postdiplomske studije i postdoktorske istraživačke pozicije. Tu su pojedinačni doprinosi najvažniji i neophodni za napredak u karijeri, i tu se oni, kao nezavisni istraživači, u velikoj meri

**1. You are a scientist working for the economy. What does it look like when the business model is based on the achievements of your research team? And do you expect other businesses to think in that direction as well?**

Most scientists come from an academic setting they progress through post-graduate studies and post-doctoral research positions. There, individual contributions are most important and necessary for

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vrednuju na osnovu broja recenziranih publikacija i dobijenih grantova za istraživanje. Na početku svoje karijere, lično sam iz akademske zajednice prešao u industrijska istraživanja, radeći u nekoliko biotehnoloških i farmaceutskih kompanija, pre nego što sam se pridružio *Philip Morris International Research Laboratories*. Postojale su dve veoma primetne razlike u kulturi između akademskih i industrijskih naučnika. Prvo, istraživački projekti u industriji su suviše vremenski zavisni. I drugo, timski rad i multidisciplinarne interakcije postaju kritični za ukupan uspeh bilo kog projekta koji se sprovodi u komercijalnom okruženju, kako u pogledu kvaliteta projekta, tako i u pogledu vremenskih rokova. Uz jedan takav zajednički napor, u mogućnosti smo da vodimo studije koje bi bile sasvim nemoguće sprovesti u akademskom okruženju. Kao primer, nedavno smo završili dugoročnu (skoro 2 godine) *in vivo* studiju o karcinomu[1]. Ovome je doprinelo više timova, uključujući i opremu, inženjere i naučnike koji se bave aerosolom, tehničare zadužene za životinje, veterinare, naučnike i osobe odgovorne za osiguranje kvaliteta, sa ukupnim brojem aktivnih saradnika u studiji u različitim fazama koji je premašio 40 ljudi. Očekivao bih da ovo visoko kooperativno okruženje bude uobičajena tema u drugim uspešnim poslovima u timu prirodnih nauka. Upravo iz tog razloga mi u našoj organizaciji uvek ističemo visoko saradničku kulturu.

**2. Rukovodilac ste laboratorije koja se bavi *in vivo* toksikološkim ispitivanjima. Zašto se Vaša laboratorija nalazi u Singapuru?**

Od kasnih devedesetih, Singapur je dao veliki prioritet razvoju biomedicinske industrije. Ovo se desilo u obliku infrastrukturnih obaveza, kao što je nekoliko naučnih parkova, kao i kroz atraktivno finansiranje i programe grantova, podsticajno regulatorno okruženje. Ovaj pristup je privukao veliki broj istaknutih istraživača i naučnih / farmaceutskih kompanija. Sve zajedno ovo čini Singapur veoma atraktivnom lokacijom za našu kompaniju za sprovođenje istraživanja. Pozicionirani smo u živahnom i naprednom istraživačkom okruženju koje je dobro povezano sa ostatkom Azije, sa najsavremenijom opremom i velikim brojem obučenih i iskusnih „*life science*" naučnika, što je važno za posao. Ličnije rečeno, Singapur je fantastično mesto za život i podizanje porodice, a kao Kanađanin, posebno cenim tropsku klimu tokom cele godine.

**3. Na kojim životinjama vršite ispitivanja i kojih principa laboratorijske prakse se pridržavate?**

U našem objektu obično sprovodimo dve glavne vrste studija prvenstveno koristeći miševe i pacove. Bezbednosne toksikološke studije procene sprovode se na novim hemijskim entitetima ili aerosolima sa

career progression where they, as independent researchers, are largely evaluated based on the number of peer-reviewed publications and accepted research grants. Early in my career I personally had moved out of academia to industrial research, working in several biotechnology or pharmaceutical companies before joining Philip Morris International Research Laboratories. There were two very noticeable differences in culture between academic and industrial scientists. First, projects for industry research are much more time dependent. And second, teamwork and multidisciplinary interactions become critical to the overall success of any project conducted within a commercial setting, both in terms of project quality as well as in timelines. With such a collective effort, we are able to conduct studies which would be quite impossible in an academic setting. As an example, we had recently completed a long-term (nearly 2 years) in vivo cancer study[1]. This had contributions from multiple teams, including facilities, aerosol engineers, aerosol scientists, animal technicians, veterinarian, scientist, and quality assurance, with the total number of active contributors in the study at various stages well exceeding 40 people.

I would expect this highly cooperative environment to be a common theme in other successful businesses within the life sciences team. It is for this reason that we in our function always emphasize a highly collaborative culture.

**2. You are a head of a laboratory that deals with in vivo toxicological tests. Why is your laboratory located in Singapore?**

Since the late 1990's, Singapore has had placed a high priority on the development of its biomedical industry. This has occurred in the form of infrastructural commitments, such as several science parks, as well as through attractive funding and grant programs, and a supportive regulatory environment. This approach attracted a large number of prominent researchers and life science / pharmaceutical companies. Collectively this makes Singapore a very attractive location for our company to conduct research. We are positioned within a vibrant and thriving research environment that is well connected to the rest of Asia, with state-of-the-art facilities, and a high depth of skilled and experienced life science workers which is important for recruitment. On a more personal note, Singapore is a fantastic place to live and raise a family, and as a Canadian, I especially appreciate the year-round tropical climate.

**3. Which animals do you perform tests on, and which principles of laboratory practice do you follow?**

At our facility, we typically conduct two main types of studies primarily using mice and rats. Safety toxicological assessment studies are conducted on novel

[1]Reduced Chronic Toxicity and Carcinogenicity in A/J Mice in Response to Life-Time Exposure to Aerosol from a Heated Tobacco Product Compared with Cigarette Smoke

ciljem da se proceni doza ili vremenski zavisni profil toksičnosti, bilo na sistemu respiratornog trakta, bilo sistemski, nakon ponovljene izloženosti. Takve studije su važne za pripremu dokumenata za podnošenje regulatornim organima, kao što je američka Agencija za hranu i lekove (FDA), i sprovode se prema standardizovanim smernicama za testiranje. Pored toga, procenjujemo aerosole na različitim životinjskim modelima bolesti, sa naglaskom na bolesti povezanih sa pušenjem, kao što su rak pluća, hronična opstruktivna bolest pluća i kardiovaskularne bolesti. Takve studije se sprovode da bi se procenio specifični rizik od razvoja bolesti, na primer upoređivanje uticaja aerosola iz novih kategorija bezdimnih proizvoda u odnosu na dim cigareta. Naš objekat je akreditovan za sprovođenje studija u sladu sa standardom dobre laboratorijske prakse (DLP). To znači da smo deo Organizacije za ekonomsku saradnju i razvoj (OECD) za uzajamno prihvatanje podataka u kontekstu regulatornog prihvatanja, multilateralnog sporazuma koji omogućava da se rezultati nekliničkih studija bezbednosti, proizvedeni u skladu sa podacima i integritetom principa dobre laboratorijske prakse, mogu deliti u zemljama članicama OECD-a ili pridruženim državama. Kao deo ovoga, na godišnjem nivou imamo reviziju studija i objekata. Pored toga, takođe smo akreditovani od strane Američke asocijacije za akreditaciju nege laboratorijskih životinja (AAALAC), koja prepoznaje našu ustanovu u kojoj je postignut najviši nivo nege životinja i etičkog tretmana životinja, što uključuje višestruke inspekcije i revizije objekata. Obe akreditacije su važne i predstavljaju naš naglasak i na naučnu izvrsnost i kvalitet podataka, kao i na etičku brigu i upotrebu istraživačkih životinja.

**4. Možete li da podelite sa nama rezultate istraživanja koja su po Vašem mišljenju najinteresantnija?**

Na ovo pitanje je teško odgovoriti, pošto smo sproveli toliko važnih i zanimljivih studija u proteklih 12 godina.

chemical entities or aerosols with the aim to assess the dose or time-dependent toxicity profile, either to the respiratory tract system, or systemically, following repeated exposure. Such studies are important for the preparation of regulatory submission documents, such as for the U.S. FDA, and are conducted following standardized testing guidelines.

In addition, we assess aerosols in various animal models of disease, with emphasis on the tobacco related diseases such as lung cancer, chronic obstructive pulmonary disease, and cardiovascular disease. Such studies are conducted to assess disease specific risk, for example comparing aerosols from novel smoke-free product categories relative to that from combustible cigarette smoke.

Our facility is accredited to conduct studies to Good Lab Practices (GLP) standard. This means that we are part of the Organization for Economic Co-operation and Development's(OECD) mutual acceptance of Data in the context of regulatory acceptance, which is a multilateral agreement to allow results of non-clinical safety studies, produced to data and integrity principles of Good Laboratory Practice, to be shared across OECD member states or adherent states. As part of this, we are subject to both study and facility-based audits on an annual basis. In addition, we are also accredited by the American Association for Accreditation of Laboratory Animal Care (AAALAC), which recognizes our facility as achieving the highest level of animal care and ethical treatment of animals, which involves multiple facility inspections and audits. Both accreditations are important, and represent our emphasis on both scientific excellence and data quality, as well as on the ethical care and use of research animals.

**4. Can you share with us the results of the tests which in your opinion are the most interesting?**

This is a difficult question to answer, as we have conducted so many important and interesting studies over

U stvari, objavili smo preko 30 recenziranih članaka[2] i poglavlja u knjigama, i imamo preko 500 citata. Procenjivali smo aerosole proizvedene iz nekoliko naših bezdimnih proizvoda na različitim životinjskim modelima bolesti, kao što su kardiovaskularne bolesti, hronična opstruktivna bolest pluća i kancer. U ovim modelima, tretman pozitivne kontrole – izlaganje dimu cigareta, rezultiralo je razvojem i progresijom nekoliko važnih indikatora bolesti zavisnih od vremena i koncentracije, uključujući plućni emfizem, narušavanje plućne funkcije, zapaljenje pluća, formiranje aterosklerotskog plaka i genezu tumora. Alternativno, aerosoli iz bezdimnih proizvoda koji se procenjuju, isporučeni životinjama u istoj koncentraciji nikotina kao grupe izlagane dimu cigareta, nisu pokazali nikakvu očiglednu promenu ni u jednom od ovih parametara u odnosu na kontrolne životinje tretirane svežim vazduhom, što ukazuje da su ovi proizvodi pokazali smanjeni rizik od razvoja bolesti u odnosu na dim cigarete u ovim modelnim sistemima. Bilo je veoma uzbudljivo videti ove rezultate reprodukovane u više studija, koristeći različite platforme bezdimnih proizvoda.

**5. Kakav je značaj *in vivo* testiranja na životinjama kada su u pitanju duvanski proizvodi?**

Svi mi u *Philip Morris International Research Laboratories* shvatamo da postoji zabrinutost javnosti o istraživanju na životinjama, koje se sprovodi u više industrija, uključujući i duvansku industriju. Gde god je to moguće, nastojimo da zamenimo testiranje na životinjama alternativama koje ne uključuju životinje, kao što je korišćenje *in siliko* modelovanja ili *in vitro* studije. Takođe smo aktivni u razvoju alternativnih modela testiranja na životinjama. Ovo osigurava da se obim testiranja na životinjama koja se na kraju sprovode drži na apsolutnom minimumu i uzima se u obzir samo kada je potrebno, na primer, za regulatorne zahteve. Budući da smo AAALAC akreditovani objekat, mi obezbeđujemo apsolutno najviši standard za dobrobit i negu svih životinja koje borave u našem objektu. Naš objekat se striktno pridržava „3R" principa istraživanja na životinjama: zameniti, smanjiti i poboljšati. Zamena znači da koristimo alternativno testiranje bez životinja gde god je to moguće ili prikladno. Smanjenje se vrši korišćenjem minimalnog broja životinja za testiranje, koliko je neophodno da bi se dobili validni rezultati. A poboljšanje je sprovođenje svih studija korišćenjem najmanje invazivnih mogućih sredstava. Za ovo imamo dobro obučeno osoblje na svim nivoima, koje se stalno usavršava najnovijim tehnikama kako bismo upravljali životinjama i eksperimentima na najbolji mogući način.

the past 12 years. In fact, we have contributed to over 30 peer-reviewed articles[2] and book chapters, and over 500 citations. We have evaluated the aerosols produced from several of our smoke-free products in different animal models of disease, such as cardiovascular disease, chronic obstructive pulmonary disease, and cancer. In these models, the positive control treatment, cigarette smoke exposure, resulted in a time and concentration-dependent development and progression of several important disease indicators including pulmonary emphysema, pulmonary function, pulmonary inflammation, atherosclerotic plaque formation and tumor genesis. Alternatively, aerosols from the smoke-free products under evaluation, delivered to the animals at the same nicotine concentrations as the cigarette smoke groups did not show any obvious change in any of these parameters relative to the control, fresh air-treated animals, and indicative that these products had a reduced disease risk relative to cigarette smoke in these model systems. It was very exciting to see these results reproduced in study after study, using various different smoke-free product platforms.

**5. What is the significance of in vivo animal testing when it comes to tobacco products?**

We at Philip Morris International Research Laboratories all understand that there is public concern about animal research as conducted in multiple industries, including the tobacco industry. Wherever possible, we strive to replace animal testing with non-animal alternatives, such as using in silico modelling, or in vitro studies. We are also active in the development of alternatives to animal testing. This ensures that the volume of animal testing which is ultimately conducted is kept to the absolute minimum and considered only when required, for example, for regulatory submissions. Being an AAALAC-accredited facility, we ensure the absolute highest standard for welfare and care of all animals which reside in our facility. Our facility strictly adheres to the '3R's' principles of animal research: replace, reduce, and refine. Replacement means that we use alternative, non-animal testing wherever possible or appropriate. Reduction is performed by using the minimal numbers of animals for testing as needed to provide valid results. And refinement is the conduct of all studies using the least invasive means possible. For this, we have well trained staff at all levels all constantly updated on the latest techniques in order to manage the animals and the experiments in the best possible manner.

[2]Evaluation of the Tobacco Heating System 2.2. Part 4: 90-day OECD 413 rat inhalation study with systems toxicology endpoints demonstrates reduced exposure effects compared with cigarette smoke
An 8-month systems toxicology inhalation/cessation study in Apoe-/- mice to investigate cardiovascular and respiratory exposure effects of a candidate modified risk tobacco product, THS 2.2, compared with conventional cigarettes
Reduced Chronic Toxicity and Carcinogenicity in A/J Mice in Response to Life-Time Exposure to Aerosol from a Heated Tobacco Product Compared with Cigarette Smoke

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