
# MSD's Longstanding Commitment to Preventing and Treating Infectious Diseases

*MSD's strategy to address antimicrobial resistance, a global public health threat*

Vaccines and antibiotics have revolutionized infectious disease prevention and treatment. For decades, MSD has played a significant role in vaccine and antibiotic research and development (R&D). Our medicines and vaccines span multiple infectious disease categories in both human and animal health. Today, MSD is one of only a few large pharmaceutical companies that has sustained a focus in R&D to prevent and treat bacterial infections.

### The Growing Threat of Antimicrobial Resistance (AMR)

Bacteria resistant to antibiotics are becoming more common, reducing the effectiveness of treatments for infections and jeopardizing health care gains to society, such as those in organ transplantation, cancer chemotherapy and major surgery. According to the World Health Organization (WHO)[1], the health and economic consequences of antibiotic resistance are considerable and costly, making it a serious threat to societal health.

Recognizing the need to address this global health threat, MSD joined more than 80 biopharmaceutical, generic medicines and diagnostic companies, as well as key trade associations, in signing a declaration at the 2016 World Economic Forum that sets out bold commitments and calls on governments and industry to take joint action against AMR.

1. *Antimicrobial resistance: global report on surveillance* (2014)

***"MSD remains deeply committed to working with governments, health care providers, patients and others to drive antibiotic innovation, promote appropriate use and enhance access for patients."***

Kenneth C. Frazier, Chairman and Chief Executive Officer

## MSD is Taking Action to Combat Antimicrobial Resistance

As a global health care leader, we are investing our resources and expertise to drive innovation that promotes human and animal health and wellness by preventing and treating infections.

**Leading in infection prevention** through the development and production of vaccines to prevent infections and reduce antibiotic use

**Driving innovation** to research, develop and commercialize new treatments and antibiotic alternatives to address important unmet medical needs

**Advancing antimicrobial stewardship (AMS) programs** to support the appropriate use of antibiotics and slow the pace of resistance

**Supporting global surveillance and awareness** of AMR through our Study for Monitoring Antimicrobial Resistance Trend (SMART) and AMR/AMS awareness programs

**Advocating for policy solutions** to address the global challenges limiting development of and access to new antibiotics, vaccines and diagnostics needed to combat AMR

# Leading in Infection Prevention

## MSD continues to develop and deliver a broad portfolio of human and animal vaccines to prevent infection and reduce the need for antibiotic therapy.

***"Vaccines are a powerful force of global health. MSD is on a mission to ensure that more people can access our vaccines, regardless of where they live or their financial circumstances."***

Mike Nally, President of MSD Vaccines

Universal coverage with a pneumococcal conjugate vaccine could avert up to **11.4 million days of antibiotic use per year** in children younger than five years – a **47% reduction** in the amount of antibiotics used for pneumonia caused by *Streptococcus pneumoniae*[2].

2. Laxminarayan R, Matsoso P, Pant S, Brower C, Røttingen J, Klugman K, Davies S, Access to effective antimicrobials: A worldwide challenge, Antimicrobials: access and sustainable effectiveness, *Lancet*, 2016, 387: 168–75.

Increasing vaccine population coverage has the potential to significantly reduce antibiotic use by preventing diseases in both humans and animals.

MSD is dedicated to researching and producing vaccines to address the public health burden of disease. We contribute to the vision of United Nations Sustainable Development Goal 3: Ensure healthy lives and promote well-being for all at all ages. In particular, we are addressing two of the leading preventable causes of death for children younger than five in the developing world – diarrhea and pneumococcal diseases.

Additionally, we have multiple programs evaluating early stage vaccine candidates, including V114, an investigational 15-valent pneumococcal vaccine designed to protect against *S. pneumoniae* infection.

MSD Animal Health is the world's largest producer of vaccines for animals and has invented and developed a broad array of vaccine products, as well as anti-infective and anti-parasitic therapies to advance animal health. Vaccination and other strategies are in development to reduce foodborne infections caused by *Salmonella* and *Campylobacter.*

**Hilleman Laboratories**, named after MSD scientist and vaccines pioneer, Dr. Maurice Hilleman, is a nonprofit R&D joint venture between MSD and the Wellcome Trust. It was founded in 2009 with a mission to develop affordable vaccines for global health.

In March 2016, MSD Animal Health's newly acquired **HarrisVaccines** was granted first-of-its-kind approval by U.S. Department of Agriculture (USDA) for its innovative production platform that allows for herd-specific, custom vaccines for animals. The same RNA particle technology received conditional license approval for porcine epidemic diarrhea (PEDv) and the H5 avian influenza vaccines.

## To keep both humans and animals healthy and minimize antibiotic use, MSD commits to:

1. Continue to invest in R&D for innovative vaccines and preventive options that reduce dependence on antibiotics and help combat AMR.
2. Develop and deliver affordable, life-saving vaccines that address global public health priorities, including heat-stable rotavirus and oral cholera vaccine candidates.
3. Continue to work with governments, health care professionals and patients to promote the value of vaccination as a cost-effective intervention.
4. Build upon MSD Animal Health's role as the world's largest manufacturer of vaccines for animals by investing in new technology, such as RNA particle technologies, to address emerging diseases.

# Driving Innovation

## MSD makes significant investments in infectious disease R&D to address unmet public health needs with innovative treatment options.

MSD has already contributed **two novel antibiotics** to the Infectious Disease Society of America's 10x'20 initiative: **SIVEXTRO** (tedizolid) and **ZERBAXA** (ceftolozane/tazobactam). These are in addition to other MSD antibiotics: **DIFICID** (fidaxomicin) and **CUBICIN** (daptomycin).

In 2015, MSD scientists published **more than 30** peer-reviewed journal articles on antimicrobial-related studies in leading journals, including *Nature* and *PLOS*.

Since 2009, MSD has invested **€21 million** through Fundación Medina (Granada Spain), a non-profit research organization focused on the discovery of new molecules with the potential to treat infectious diseases. In April 2016, MSD donated **over 74,000** natural product-producing strains of microorganisms to aid research.

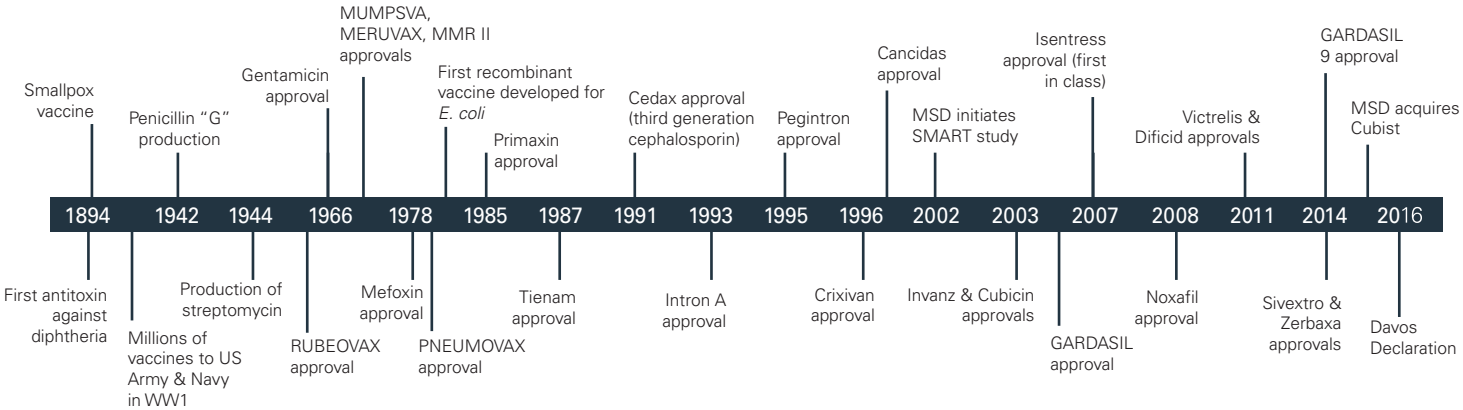
Anti-infective research remains a key area of focus for MSD. We continue to invest in antimicrobial and vaccine R&D, and have collaborations spanning discovery through late-stage clinical development. In addition to MSD's broad anti-infective portfolio of marketed products indicated for the treatment of serious infections, our investigational pipeline includes candidates targeting Gram-negative pathogens and other organisms prioritized by health authorities:

- **Carbapenem-resistant *Enterobacteriaceae***: MK-7655a is an investigational combination of a novel ß-lactamase inhibitor and imipenem/cilastatin (an approved carbapenem antibiotic) that is currently being evaluated in Phase 3 trials. MSD is currently studying MK-7655a for the treatment of serious infections including complicated intra-abdominal infections, complicated urinary tract infections, and hospital-acquired pneumonia.
- ***Clostridium difficile***: Bezlotoxumab is an investigational antitoxin currently being evaluated by regulatory bodies for the prevention of *Clostridium difficile* infection (CDI) recurrence. Bezlotoxumab is not an antibiotic, but it has the potential to reduce the need for multiple rounds of antibiotics to treat recurrent CDI.

Additionally, **ZERBAXA** and **SIVEXTRO** are being studied in Phase 3 trials for the treatment of hospital/ ventilator-acquired bacterial pneumonia.

Nearly 200,000 people die each year from multi-drug resistant tuberculosis (TB) and new treatments are desperately needed. Through the **TB Drug Accelerator Program**, MSD is sharing compound libraries and relevant data with scientists around the world. To date, almost **3 million small molecules** have been screened for activity. In collaboration with others, we are further evaluating several candidates identified through initial screening.

## For more than 80 years, MSD has played a significant role in antimicrobial development, extending back to the early days of antibiotic therapy.



## Ensuring Further Antimicrobial Innovation

Sustaining investment in antimicrobial R&D poses significant challenges. Novel antibiotics are undervalued relative to their societal benefits and are often set aside in an effort to preserve their effectiveness. To stimulate R&D efforts targeting anti-infective priority areas, governments and payers need to implement policies that promote sustainable investment in ongoing innovation to combat AMR and drive appropriate use.

Incentive proposals will need to address the lack of financial return for novel antibiotics in current reimbursement systems, as well as build robust "push and pull" mechanisms to stimulate investment into the R&D of antibiotics that are currently in early clinical and pre-clinical development. Lack of action to address these reimbursement challenges will undermine confidence in investing in antibiotic R&D while novel incentive mechanisms are explored and implemented.

We believe that market-based incentive models best allocate scarce resources and reward successful innovation. Market-based models that build on existing systems and effectively drive innovation across other therapeutic areas can be refined to incentivize and sustain antibiotic innovation and reinforce AMS. Interventions will need to be tailored to work within the varied structures of countries' health systems.

There is not a "one size fits all" solution to incentivizing antibiotic innovation. The range of incentives that MSD supports includes:

- **Reimbursement reform:** Efforts to establish procedures that reimburse hospital-administered antibiotics separately from bundled hospital payments based on patient diagnoses, as a way to ensure that their use is driven only by clinical, not economic, considerations;
- **Tax credits:** Refundable tax credits for antibiotic R&D to stimulate pre-clinical and clinical research by biopharmaceutical companies;
- **Novel incentive models:** Exploration of models that reduce the proportion of manufacturer revenue from the volume of antibiotic sales, while still providing a competitive return on investment. These include models based on predictable and reliable **"market entry rewards"** in key markets such as the US and EU, and models based on **transferable marketing exclusivity.**

MSD supports legislation and regulation to enable regulatory authorities to streamline, accelerate and defray the cost of clinical trials required for regulatory review and approval of antibiotics, and for new indications for existing antibiotics to address serious infections. We also strongly encourage the harmonization of clinical trial guidance across international regulatory agencies to expedite registration.

## Supporting Stewardship and Access

Industry, governments and other stakeholders must collaborate closely to develop and implement programs to support appropriate use of and access to antibiotics. Policies intended to spur innovation need to be coupled with AMS and access measures that ensure patients receive appropriate treatment.

MSD is involved in several public-private partnerships to improve clinical trial design, recruitment and the regulatory path, including the **Duke Clinical Trials Transformation Initiative** and the Foundation for the National Institutes of Health **Biomarkers Consortium Hospital-Acquired Bacterial Pneumonia/Ventilator-Associated Bacterial Pneumonia (HABP/VABP) working group**.

MSD actively participates in international and country-level initiatives to explore how value-based reimbursement and other models can incentivize sustainable investment in antimicrobial development. We are a member of **DRIVE-AB,** an industry collaboration focused on the reduction of AMR through responsible antibiotic use and the development of new economic models to incentivize antibiotic R&D.

# To spur innovation and deliver critical new antimicrobial therapies, MSD commits to:

1 Continue to drive innovation and deliver new antimicrobial treatment and prevention options to meet unmet medical needs and improve patient outcomes.

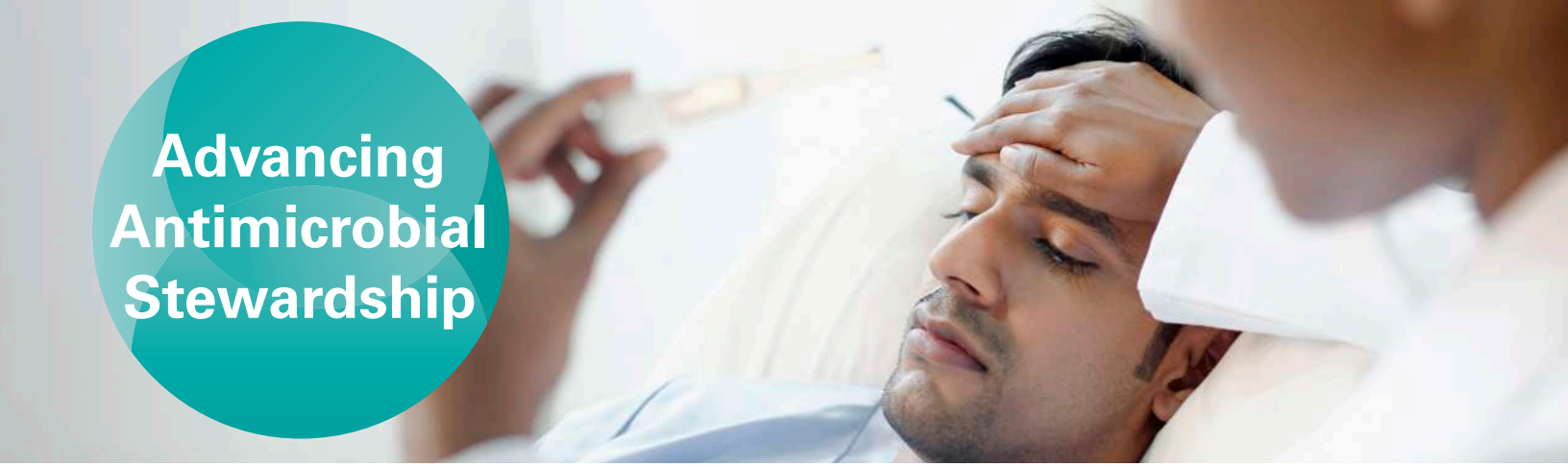
2 Advocate for incentive models that support use of novel antibiotics across the product lifecycle, including appropriate reimbursement within existing payment systems and novel "push" and "pull" mechanisms.

3 Partner with governments and other stakeholders to develop new economic models that create a sustainable market for antibiotics and promote investment in R&D

4 Facilitate antimicrobial research by providing the broad scientific community access to research tools and information and participate in collaborative efforts to advance early research through WIPO Re:Search, the TB Drug Accelerator and our partnership with Fundación Medina.

5 Develop an access strategy specific to MSD's antimicrobial portfolio to enhance access to our novel antibiotics globally while limiting inappropriate use.

# Advancing Antimicrobial Stewardship



MSD promotes patient-centered AMS to slow the emergence of resistance, prolong the activity of antimicrobials and improve patient outcomes and population health.

Since 2008, MSD has worked with **more than 500 hospitals in 26 countries** to develop and implement AMS programs. More than **10,000 health care providers** and **more than 400 locally tailored treatment pathways** have been implemented. In Latin America, MSD has partnered with CIDEIM, an independent, non-profit microbiology/infectious disease research institute to serve as an AMS Center of Excellence, providing training, guidance and support to hospitals across the region.

Over the past few years, MSD has committed **$100 million** to a water-infrastructure improvement initiative to install Active Pharmaceutical Ingredient (API)-treatment technology at our facilities. This assures that factory discharges do not contain residual pharmaceutical products that may present a risk to human health or the environment.

We support AMS efforts designed to improve the appropriate use of antimicrobials, including those that encourage the informed selection of the optimal dose, duration of therapy, route of administration, de-escalation of treatment and care setting.

Beyond clinical AMS programs, MSD supports a broad range of OneHealth activities across the company, which promote the appropriate use of antibiotics in humans and animals, as well as reduce the environmental impact from the production of antibiotics.

MSD subsidiary **ILÚM Health Solutions** offers health systems a specialized, technology-enabled service designed to address the unique challenges of infectious diseases. This service facilitates data-driven AMS programs and promotes early recognition and appropriate intervention through adherence to hospital pathways.

Through the **Global Health Innovation Fund**, MSD has invested over **US$16 million** (37% stake) in **Opgen** to develop a rapid DNA testing technology to quickly identify drug-resistant bacteria. The rapid testing allows hospitals or public health experts to identify and more quickly administer the appropriate treatment to patients who are found to be infected.

***"The rise in infections that are resistant to current antibiotics has become one of the world's most pressing public health problems. We are proud to reaffirm our longstanding commitment to develop new therapeutics to fight infectious diseases, and to continue to collaborate with others to support antimicrobial stewardship to help slow the rate of emerging resistance."***

Dr. Julie Gerberding, Executive Vice President and Chief Patient Officer

MSD has provided significant grant funding to advance relevant AMS work, including:

- Approximately **$1 million** to support the Centers for Disease Control and Prevention (CDC)/CDC Foundation and Duke University's two-year collaborative project to develop standardized patient safety outcomes measures that are meaningful and practical for hospital AMS programs;
- Funding and subject matter expertise to support the development of the National Quality Forum's AMS Playbook providing practical guidance for acute care facilities to implement AMS programs;
- Over **$1.5 million** since 2013 in funding for 18 investigator-initiated studies on AMS unrelated to MSD products; and
- More than **$3 million** in independent educational grants related to AMS in 2015 to over 20 US organizations, including a grant to support the development of a new annual meeting focused on improving the quality of AMS research.

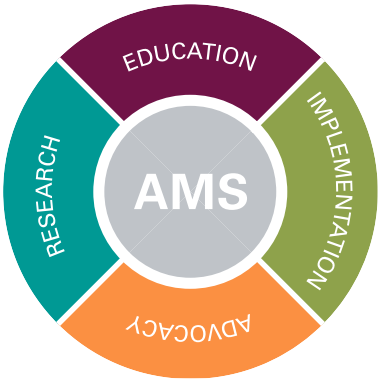
**Supporting AMS in Animal Health**

MSD Animal Health supports the responsible use of antibiotics to improve and maintain the health and welfare of animals. Clinical research has shown that antibiotics, when used appropriately, are effective tools to manage disease in animal populations, protect human health by reducing the spread of zoonotic disease and are a critical component to ensuring a safe food supply.

MSD Animal Health recently added the Whisper® Veterinary Stethoscope System to its portfolio of vaccines and pharmaceutical products for the cattle industry. This technology can be used to quickly measure the severity of Bovine Respiratory Disease so that an appropriate treatment can be started to improve the health of the infected animal while circumventing the need for prophylactic treatment of the herd.

MSD Animal Health has also launched the ResPig® App and a dedicated website. This innovative App and Web-based platform identify areas of improvement, cost and potential outcomes of Porcine Respiratory Disease Complex, as well as provide control and prevention strategies specific to a farm's needs.

MSD Animal Health has partnered with veterinarians and poultry producers to ensure an early start on disease prevention to maintain healthy flocks. The Convenience Program® is a training-based program designed to help poultry producers optimize vaccination processes and improve chick quality.




MSD advances AMS to improve patient outcomes, population health, and value of care.

# To promote AMS, MSD commits to:

1 Expand its support for the Centers of Excellence AMS Program from 521 hospitals in 26 countries to 1,000 hospitals in 40 countries by 2019.

2 Create a global network for AMS training and support with 11 Centers of Excellence.

3 Support education on AMS, including specific information regarding responsible and appropriate use of our antimicrobial medicines, for relevant MSD employees.

4 Scale up partnerships with diagnostics companies to develop antibiotic susceptibility testing and rapid diagnostics to support appropriate use of MSD's novel antibiotics.

5 Ensure our promotional activities advance antimicrobial stewardship and protect the utility of antibiotics by encouraging their correct use.

6 Explore new value-based contracting models with payers and providers.

7 Continue efforts to ensure MSD manufacturing discharges are protective of human health and the environment, as assessed by an internal Environmental Quality Criteria program established in accordance with stringent review processes. Ensure all MSD manufacturing facilities are equipped with API-treatment technology to ensure that our wastewater meets internal standards.

8 Develop at least three collaborative initiatives emphasizing AMS education, program implementation, and research in the hospital and community settings by 2019.

# Supporting Global AMR Awareness and Surveillance

## MSD is driving awareness of AMR trends to inform appropriate antibiotic and vaccine use.

Surveillance studies can yield important information for identification of trends in pathogen incidence and AMR, and provide early indicators of the emergence of resistant strains. Such studies are fundamental to establishing effective strategies for limiting the spread and defining the appropriate treatment of AMR infections. Since 2002, MSD has sponsored the Study for Monitoring Antimicrobial Resistance Trends (SMART), a worldwide surveillance study monitoring *in vitro* susceptibility patterns of clinical Gram-negative bacilli to 12 commonly-used antibiotics.

The SMART program is one of the **world's largest** programs for tracking trends in AMR. Currently, **192** hospital sites in **54** countries participate in SMART. **Over 200,000** isolates have been collected since its launch.

Bacterial samples have been collected and characterized from patients with intra-abdominal, urinary tract and lower-respiratory tract infections.

The SMART study is a valuable resource in determining pathogen prevalence and antibiotic susceptibility. It continues to provide evidence for the establishment of regulatory susceptibility breakpoints that are important to defining antibiotic susceptibility. The information collected and shared is designed to help local and global health agencies improve surveillance so they can better understand AMR trends and determine appropriate antibiotic regimens for their patients.

**Global Awareness and Education**

To improve awareness of AMR and AMS, MSD has provided an independent grant to support the development of the CIDRAP Antimicrobial Stewardship Project, a multifunctional Web-based platform that provides access to comprehensive, high-quality AMS/AMR information and educational resources on AMS practice, research, and policy. It features a dynamic, content-rich website designed to actively engage a diverse, international audience.

We have provided a grant to the Pan American Health Organization Foundation to support countries in the Latin America region to develop national action plans to combat AMR around the key pillars of the WHO Global Action Plan: awareness, surveillance, prevention, appropriate use and incentives.

## To improve global surveillance and drive awareness of AMR, MSD commits to:

1 Expand the SMART program from 54 to 59 countries and from 192 to 222 sites, with a focus on emerging markets, by 2018.

**a.** Ensure updated data is made public, including an annual report summarizing the data by region and country.

**b.** Submit at least eight publications per year to share SMART data through peer-reviewed journals.

2 Support governments and public health initatives to educate health care professionals and patients on the value and importance of appropriately using antibiotics.

3 Continue to support efforts to develop and implement national AMR action plans in support of the WHO Global Action Plan.

## Forward-Looking Statement of MSD & Co., Inc., Kenilworth, N.J., USA

This news release of MSD & Co., Inc., Kenilworth, N.J., USA (the "company") includes "forward-looking statements" within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company's management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline products that the products will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company's 2015 Annual Report on Form 10-K and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site (www.sec.gov).

MSD