What is regulatory affairs?

Regulatory Affairs (RA), also called Government Affairs, is a profession within regulated industries, such as pharmaceuticals, medical devices, energy, and banking.
Regulatory Affairs also has a very specific meaning within the healthcare industries (pharmaceuticals, medical devices, Biologics and functional foods)

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PHARMACEUTICAL DRUG REGULATORY AFFAIRS

This department is responsible for knowing the regulatory requirements for getting new products approved. They know what commitments the company has made to the regulatory agencies where the product has been approved. They also submit annual reports and supplements to the agencies. Regulatory Affairs typically communicates with one of the Centers (e.g., Center for Drug Evaluation and Research) at the FDA headquarters, rather than the FDA local district offices.

REGULATORY BODIES

Regulatory bodies such as the Food and Drugs Administration (FDA) in the USA are responsible for approving whether a drug can proceed to clinical trials and whether it should be allowed on the market. The regulatory body has to evaluate the scientific and clinical data to ensure that the drug can be produced with consistently high purity, that it has the clinical effect claimed, and that it does not have unaccepted side effects. It must also approve the labeling of the drug and the directions for its use.

In general, the regulatory body is interested in all aspects of a drug once it has been identified as a potential useful medicine .

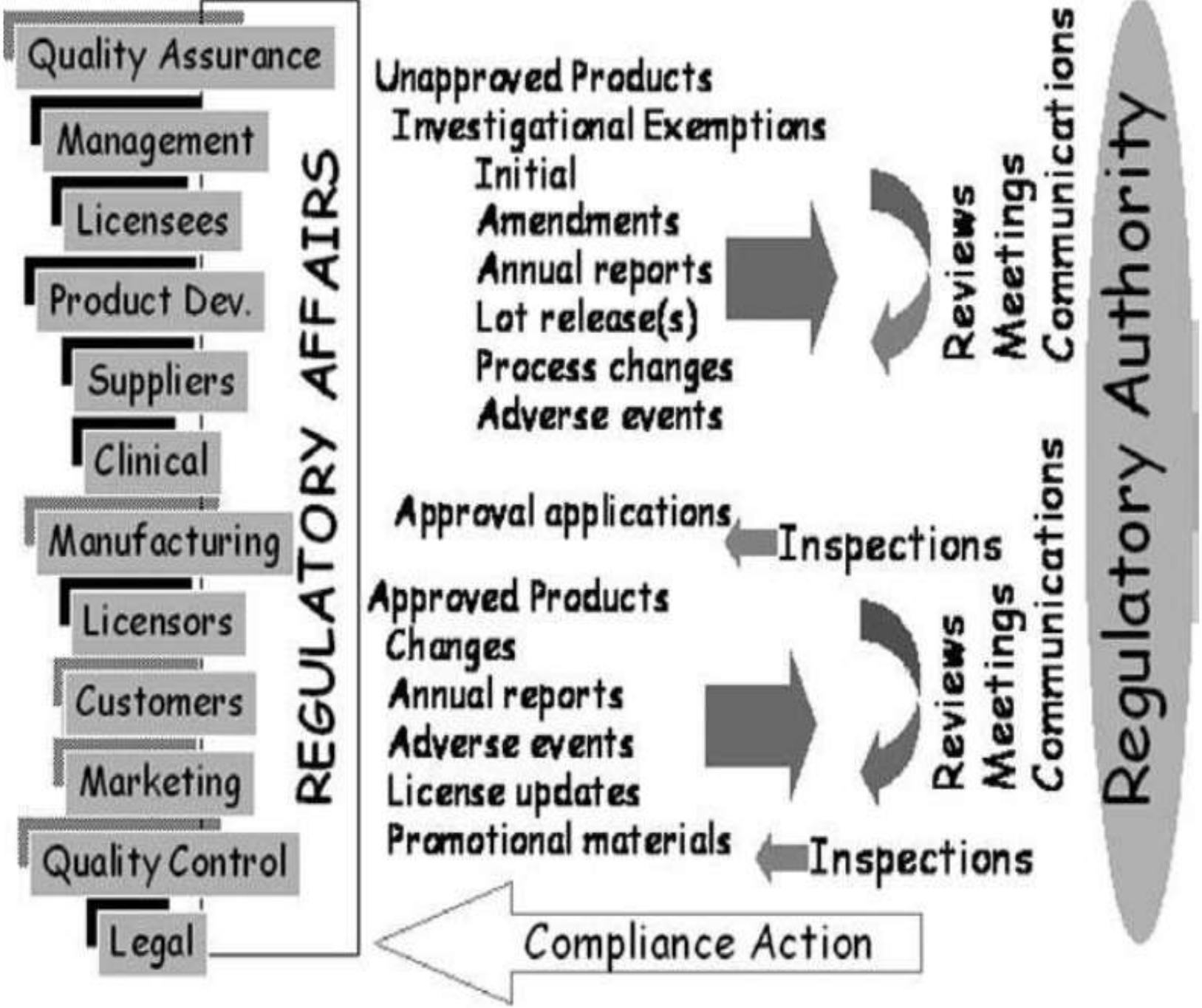

Fig 1: The spectrum of regulatory affairs

Regulatory Review: Continuity and Connection

Most large regulatory submissions involve multiple technical sections that are written by separate technical groups. As the overall "owner" of the submission, regulatory is responsible to assure the overall quality. This can usually be broken down into the concepts of continuity and connectivity.

Continuity

Earlier it was implied that regulatory should avoid writing a submission— when it comes to continuity, regulatory must take the lead in writing. Sections of the document need to flow into each other, so the document appears at some level to have one voice. This is particularly important when concepts and data from multiple sections are brought together, as in introductory sections, synopses, and summary conclusions— cut and paste doesn't cut it. The language needs to be fluid, and the order of data logical.

Connectivity

Connectivity is a concept that is seldom recognized overtly by the regulatory community, but is in fact one of our most important responsibilities when it comes to submissions.

As the owner of a submission, regulatory is really the only “person” who sees the entire document, and the document is not a linearly attached series of sections it has multiple internal cross-references and connections.

The United States **Federal Food, Drug, and Cosmetic Act** (abbreviated as **FFDCA**, **FDCA**, or **FD&C**), is a set of laws passed by Congress in 1938 giving authority to the U.S. Food and Drug Administration (FDA) to oversee the safety of food, drugs, and cosmetics.

A principal author of this law was Royal S. Copeland, a three-term U.S. Senator from New York.

In 1968, the Electronic Product Radiation Control provisions were added to the FD&C.

Also in that year the FDA formed the Drug Efficacy Study Implementation (DESI) to incorporate into FD&C regulations the recommendations from a National Academy of Sciences investigation of effectiveness of previously marketed drugs.

The act has been amended many times, most recently to add requirements about bioterrorism preparations.

The introduction of this act was influenced by the death of more than 100 patients due to a sulfanilamide medication where diethylene glycol was used to dissolve the drug and make a liquid form.

Elixir sulfanilamide

Elixir sulfanilamide was an improperly prepared sulfanilamide medicine that caused mass poisoning in the United States in 1937. It caused the deaths of more than 100 people. The public outcry caused by this incident and other similar disasters led to the passing of the 1938 Federal Food, Drug, and Cosmetic Act.

Federal Food, Drug, and Cosmetic Act

Section 408 of the Federal Food, Drug, and Cosmetic Act (FFDCA) authorizes EPA(Environmental Protection Agency) to set tolerances, or maximum residue limits, for pesticide residues on foods. In the absence of a tolerance for a pesticide residue, a food containing such a residue is subject to seizure by the government. Once a tolerance is established, the residue level in the tolerance is the trigger for enforcement actions. That is, if residues are found above that level, the commodity will be subject to seizure.

In setting tolerances, EPA must make a finding that the tolerance is "safe." Safe is defined as meaning that there is a "reasonable certainty that no harm will result from aggregate exposure to the pesticide residue." To make the safety finding, EPA considers, among other things: the toxicity of the pesticide and its break-down products, aggregate exposure to the pesticide in foods and from other sources of exposure, and any special risks posed to infants and children. Some pesticides are exempted from the requirement to have a tolerance. EPA may grant exemptions in cases where the pesticide residues do not pose a dietary risk under reasonably foreseeable circumstances.

FDC Act-10

FD&C Act Chapters I and II: Short Title and Definitions
FD&C Act Chapter III: Prohibited Acts and Penalties
FD&C Act Chapter IV: Food
FD&C Act Chapter V: Drugs and Devices
FD&C Act Chapter VI: Cosmetics
FD&C Act Chapter VII: General Authority
FD&C Act Chapter VIII: Imports and Exports
FD&C Act Chapter IX: Tobacco Products
FD&C Act Chapter X: Miscellaneous

Kefauver Harris Amendment

Drug Amendments of 1962

Long title	An act to protect the public health by amending the Federal Food, Drug, and Cosmetic Act to assure the safety, effectiveness, and reliability of drugs, authorize standardiztion of drug names, and clarify and strengthen existing inspection authority; and for other purposes.
Nickname(s)	• Drug Efficacy Amendment • Kefauver Harris Amendment
Enacted by the	87th United States Congress
Effective	October 10, 1962

“The Kefauver-Harris Drug Amendment of 1962 was known as the 'Drug Efficacy Bill.' It required drug companies to prove a drugs effectiveness before going to market. It also required companies to reveal possible side effects”.

What are the Kefauver-Harris amendments?

1. Substantial evidence from clinical trials of both safety and efficacy – the FD&C Act of 1938 only required safety data
2. FDA approval prior to marketing – previously, approval was automatic if FDA did not act on an application within 60 days
3. Adherence to current good manufacturing practices (cGMP)

Closer monitoring of clinical trials and informed consent of participants

Disclosure of side effects in advertising

Monitoring and reporting of post-marketing safety information

Kefauver Harris Amendment- **Effect**

The Kefauver Harris Amendment strengthened the U.S. Food and Drug Administration's control of experimentation on humans and changed the way new drugs are approved and regulated.
Before the Thalidomide scandal in Europe, U.S. drug companies only had to show their new products were safe. After the passage of the Amendment, an FDA New Drug Application (NDA) would have to show that a new drug was both safe and effective (previously the 1938 Food, Drug and Cosmetic Act was the main law that regulated drug safety).

Estes Kefauver considered the Amendment his "finest achievement" in consumer protection

The amendment was a response to the Thaladomide tragedy, in which thousands of children were born with birth defects as a result of their mothers taking thalidomide for morning sickness during pregnancy.

The bill by U.S. Senator Estes Kefauver, of Tennessee, and U.S. Representative Oren Harris, of Arkansas, required drug manufacturers to provide proof of the effectiveness and safety of their drugs before approval.

It should be noted that Thalidomide had not been approved for use in the United States and that the tragic birth defects that occurred were in other countries.

Frances Oldham Kelsey was the FDA reviewer who refused to approve Thalidomide for use.

New Drug Application (NDA)

•For decades, the regulation and control of new drugs in the United States has been based on the New Drug Application (NDA).

• Since 1938, every new drug has been the subject of an approved NDA before U.S. commercialization.

• The NDA application is the vehicle through which drug sponsors formally propose that the FDA approve a new pharmaceutical for sale and marketing in the U.S. The data gathered during the animal studies and human clinical trials of an Investigational New Drug (IND) become part of the NDA.

NDA-GOALS

Whether the drug is safe and effective in its proposed use(s), and whether the benefits of the drug outweigh the risks.

Whether the drug's proposed labeling (package insert) is appropriate, and what it should contain.

Whether the methods used in manufacturing the drug and the controls used to maintain the drug's quality are adequate to preserve the drug's identity, strength, quality, and purity.

DESI

(Drug Efficacy Study Implementation)

In 1968, FDA established “Drug Efficacy Study Implementation” or DESI with the aim of evaluating drugs that had not yet undergone clinical trials and review.

About 160 drugs have still not been reviewed yet are available on the market.

Known as DESI drugs, many are still used in dermatology—coal tar, sulfur, sodium sulfacetamide, and hydroquinone, among them.

DESI

(Drug Efficacy Study Implementation)

Drug Efficacy Study Implementation (**DESI**) was a program begun by the Food and Drug Administration (FDA) in the 1960s after the requirement (in the Kefauver-Harris Drug Control Act) that all drugs be efficacious as well as safe.

The DESI program was intended to classify all pre-1962 drugs that were already on the market as either effective, ineffective, or needing further study.

The Drug Efficacy Study Implementation (DESI) evaluated over 3000 separate products and over 16,000 therapeutic claims. By 1984, final action had been completed on 3,443 products; of these, 2,225 were found to be effective, 1,051 were found not effective, and 167 were pending.

OTC

Over-the-counter (OTC) drugs

Over-the-counter (**OTC**) **drugs** are medicines sold directly to a consumer without a prescription from a healthcare professional, as compared to prescription drugs, which may be sold only to consumers possessing a valid prescription.

In many countries, OTC drugs are selected by a regulatory agency to ensure that they are ingredients that are safe and effective when used without a physician's care.

OTC drugs are usually regulated by active pharmaceutical ingredients (APIs), not final products.

By regulating APIs instead of specific drug formulations, governments allow manufacturers freedom to formulate ingredients, or combinations of ingredients, into proprietary mixtures.

In many countries, a number of OTC drugs are available in establishments without a pharmacy, such as general stores, supermarkets, gas stations, etc.
Regulations detailing the establishments where drugs may be sold, who is authorized to dispense them, and whether a prescription is required vary considerably from country to country.

Ex;

1. Canada
2 .The Netherlands
3 .United States
4. United Kingdom

Category I: generally recognized as safe and effective for the claimed therapeutic indication;
Category II: not generally recognized as safe and effective or unacceptable indications;
Category III: insufficient data available to permit final classification

Drug Listing

The Drug Listing Act of 1972 requires registered drug establishments to provide the Food and Drug Administration (FDA) with a current list of all drugs manufactured, prepared, propagated, compounded, or processed by it for commercial distribution.

Drug products are identified and reported using a unique, three-segment number, called the National Drug Code (NDC), which serves as a universal product identifier for drugs. FDA publishes the listed NDC numbers and the information submitted as part of the listing information in the NDC Directory which is updated daily.


THANK YOU