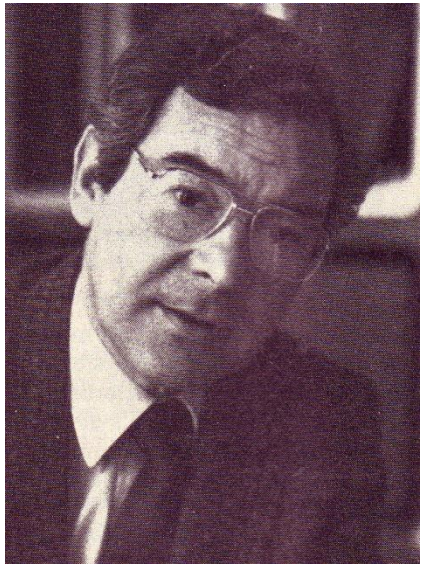
International Organization for Chemical sciences in Development

History of IOCD

Stephen Matlin

IOCD Consultation
Namur, 10-11 March 2011

Pierre Crabbé
1928-1987



1975-1987
World Health Organization
Special Programme in Human Reproduction

- **Coordinator of the Chemical Synthesis Programme for Long-acting Agents in Fertility Regulation**

- **Steering Committee member, Task Forces on Long-acting Agents in Fertility Regulation; Methods for the Regulation of Male Fertility; Fertility Regulating Agents from Plants**

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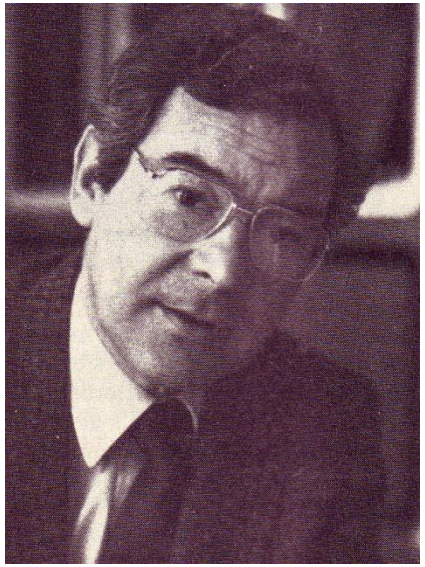
1928-1987



Injectable Contraceptive Synthesis: An Example of International Cooperation

Pierre Crabbé, Egon Diczfalusy, Carl Djerassi

Summary. Since many contraceptives appropriate for use in developing countries are not of major interest to the pharmaceutical companies in developed countries, the World Health Organization has sponsored a program whereby contraceptives are developed outside the traditional pharmaceutical industry channels. This program might serve as a model for the development of other drugs or even pesticides.

Until now pharmaceutical companies have played the dominant role in the field of chemical contraception because of the availability, within one organization, of the wide array of disciplines needed to bring such an agent to the general public (*1*). During the past decade, however, the pharmaceutical industry has reduced, on an absolute and relative basis, its research efforts in the contraceptive field (*2*). This is particularly true with regard to contraceptive methods that would be appropriate in developing countries but of relatively little interest in highly developed ones. For example, there is a great demand for long-lasting, injectable steroid contraceptives in many lesser developed nations, but the only two widely available agents (Depo-Provera and norethisterone enanthate) suffer from several disadvantages, one of these being that, although they were developed in the 1960's, they have still not been approved for general use as contraceptives by the U.S. Food and Drug Administration.

Initiation of Program

The development of new injectable contraceptives requires that a concerted effort be made to synthesize novel steroid compounds and subject them to thorough biological evaluation. Since such an effort was not being made by international pharmaceutical companies, the World Health Organization (WHO), as part of its Special Programme of Research, Development and Research Training in Human Reproduction, established a task force to determine whether such a development program could be launched outside the pharmaceutical industry. At a meeting at the WHO headquarters in Geneva in January 1975 (*3*), it was concluded that the development of a new, long-acting contraceptive agent would be worth combining with an effort at institution building in lesser developed countries. In this article we outline the initiation and organization of this program. The results obtained to date suggest that this program might serve as a model for other drug development programs outside the traditional pharmaceutical industry mechanism. For example, the development of drugs for such parasitic diseases as leishmaniasis, schistosomiasis, and onchocerciasis has been neglected by the pharmaceutical industry; a similar approach could also be envisaged for the creation of new pesticides.

In July 1975, a group of internationally recognized steroid chemists (*4*) with past or current experience in the pharmaceutical industry attended a meeting held under WHO auspices at Stanford University. These chemists compiled a list of approximately 150 hypothetical steroid compounds that they considered could be synthesized and should be subjected to biological screening in a program designed to uncover new and effective sustained-release injectable contraceptives. They also proposed 15 laboratories as candidates for participating in the program to synthesize new steroids. These laboratories, most of which are located in developing countries, were contacted by WHO headquarters staff to determine whether they would be receptive to the idea of participating in the program. The arrangement proposed was that WHO, in addition to supplying literature, material, and chemicals, would fund each laboratory to the extent of $10,000 to $15,000, the sole requirement being that 5-gram quantities of pure steroid would have to be delivered to WHO headquarters. Patent rights would remain with WHO.

Chemical Objectives

The objective of the chemical synthesis program was to modify chemically an active contraceptive steroid drug into a "prodrug" that would either be inactive or less active than the parent steroid. A simple and efficient way to achieve this goal is to protect the free 17-hydroxyl group of an active steroid by inserting an appropriate acid chain, thus producing the corresponding 17-ester (prodrug). When administered to humans, such a prodrug is converted into an active contraceptive agent by enzymatic hydrolysis in vivo (*5*). The rate at which the hydrolysis occurs determines whether the prodrug might be suitable for use as a long-acting, injectable contraceptive. The main goal of the program initiated in 1976 was to design novel steroid esters that could serve to enlarge the number of long-acting injectable contraceptives available to women. The strategy was typical of that used frequently in industrial organizations in that it involved the initial preparation of a number of esters of the known contraceptive agents 17α-hydroxyprogesterone, norethisterone [norethinyltestosterone (NET)], and levo-norgestrel. The list of steroid esters to be investigated has now been expanded to well over 250 compounds.

The natural male sex hormone, testosterone, was also included in the program, since esterification of its free hydroxyl group might afford potential candidates for an injectable male contraceptive. NET was selected as a potential progestogen, since laboratory and clinical experience has shown that it is one of the safest progestogens available and is no longer protected by patents. Levo-norgestrel, although still covered by patents, was chosen because of its high progestational potency. It is thus a good candidate for conversion into long-acting derivatives by esterification.

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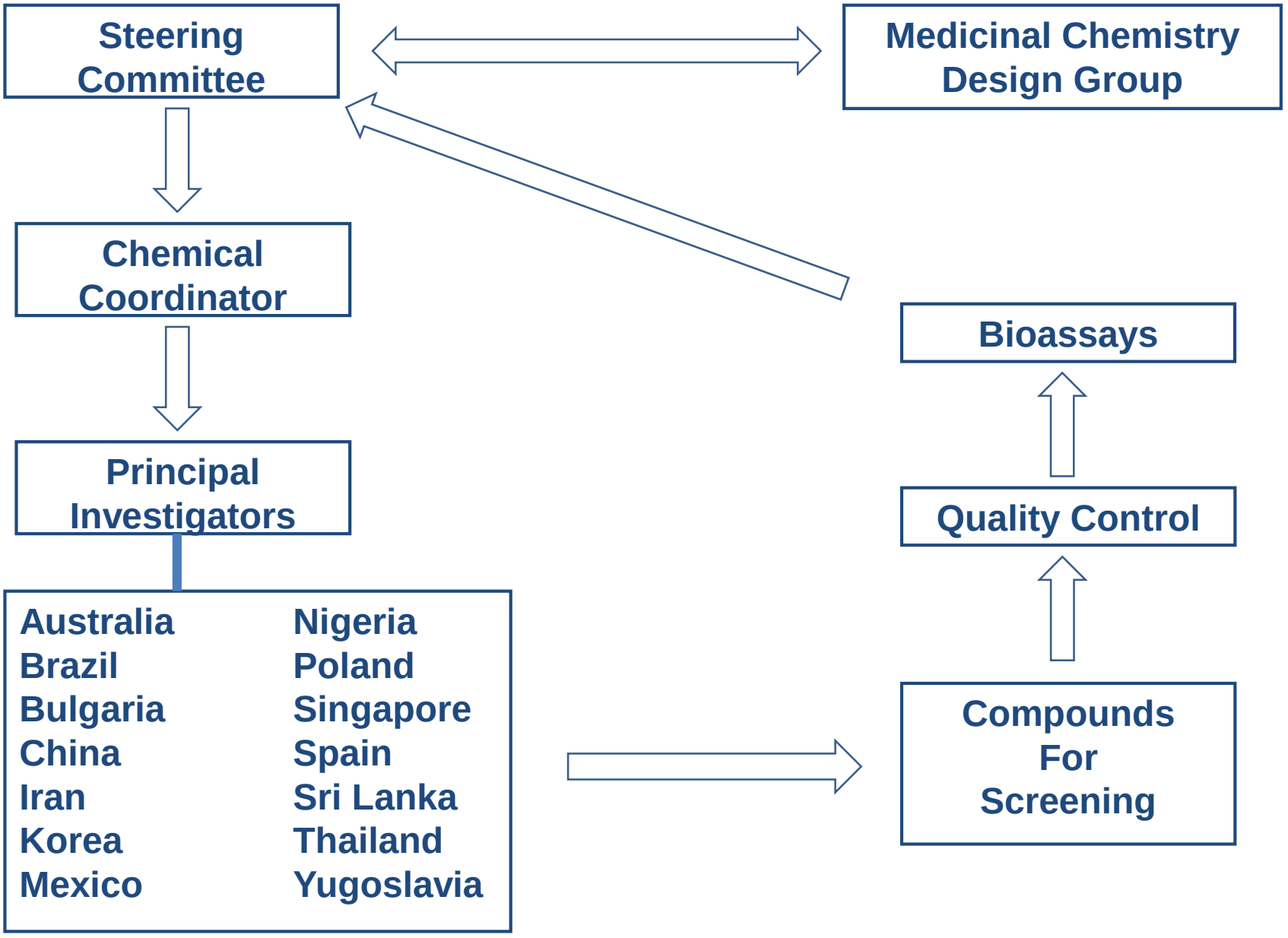
***Science*, 1983, 209, 992-4**

WHO Task Force on Long-Acting Agents for Fertility Regulation



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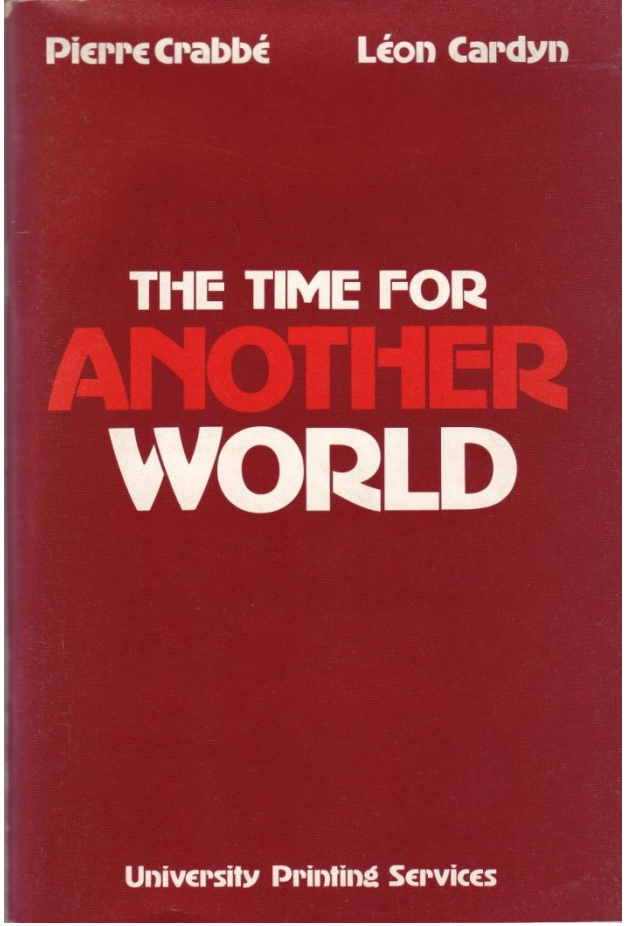
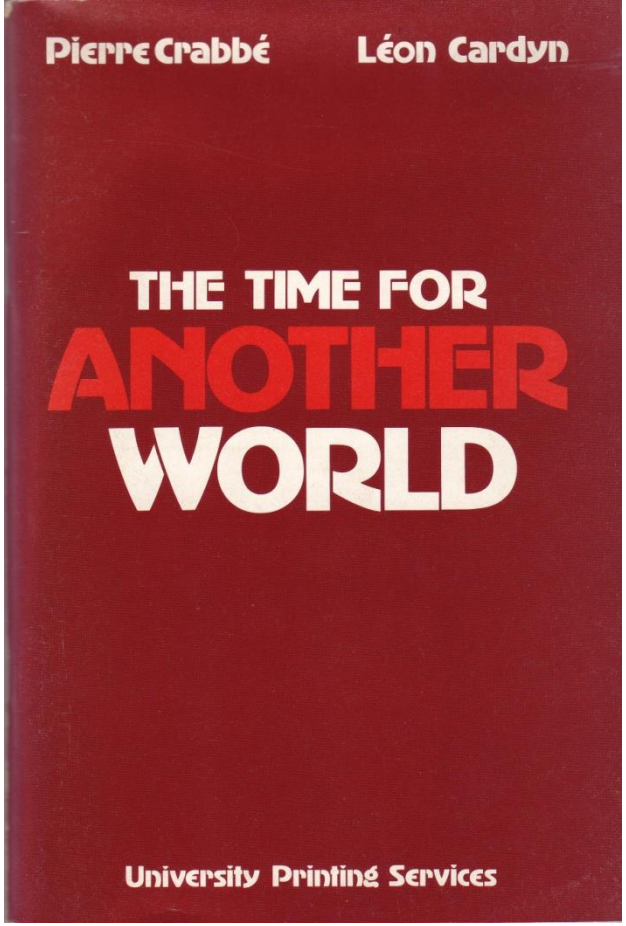


The greatest shame of our time is still to accept that every day tens of thousands, perhaps one hundred thousand people continue to die of hunger.

Pierre Crabbé , Léon Cardyn, *The Time for Another World*
University Printing Services, Columbia, Missouri, USA, 1983

Pierre Crabbé
1928-1987



The power of will is a fundamental human quality leading to success. Some dynamic individuals, usually demanding for themselves, are also demanding for others living with them and working for them. They have a strong belief that people have more in themselves and are capable of achieving more than they realize.

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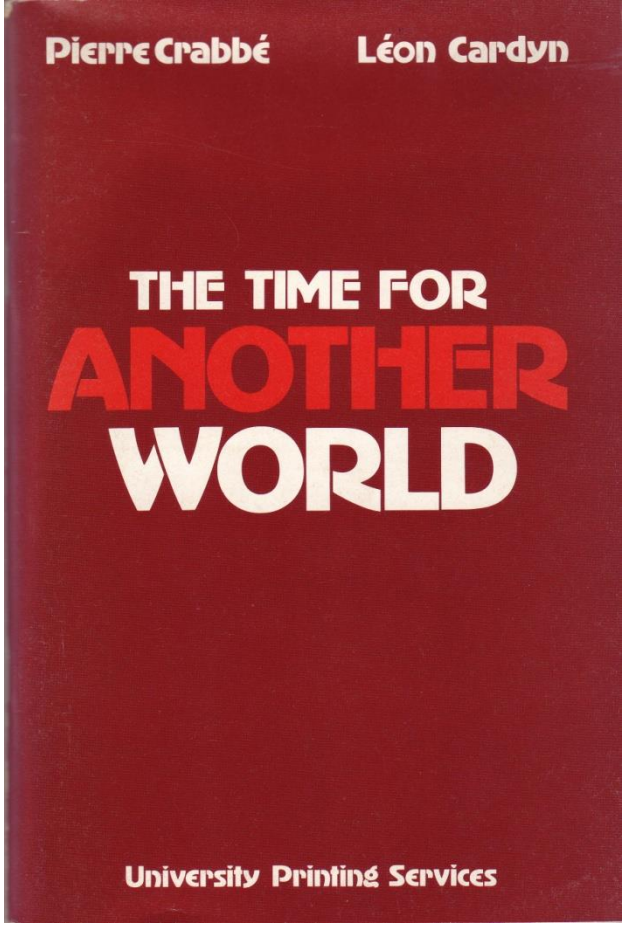
1928-1987

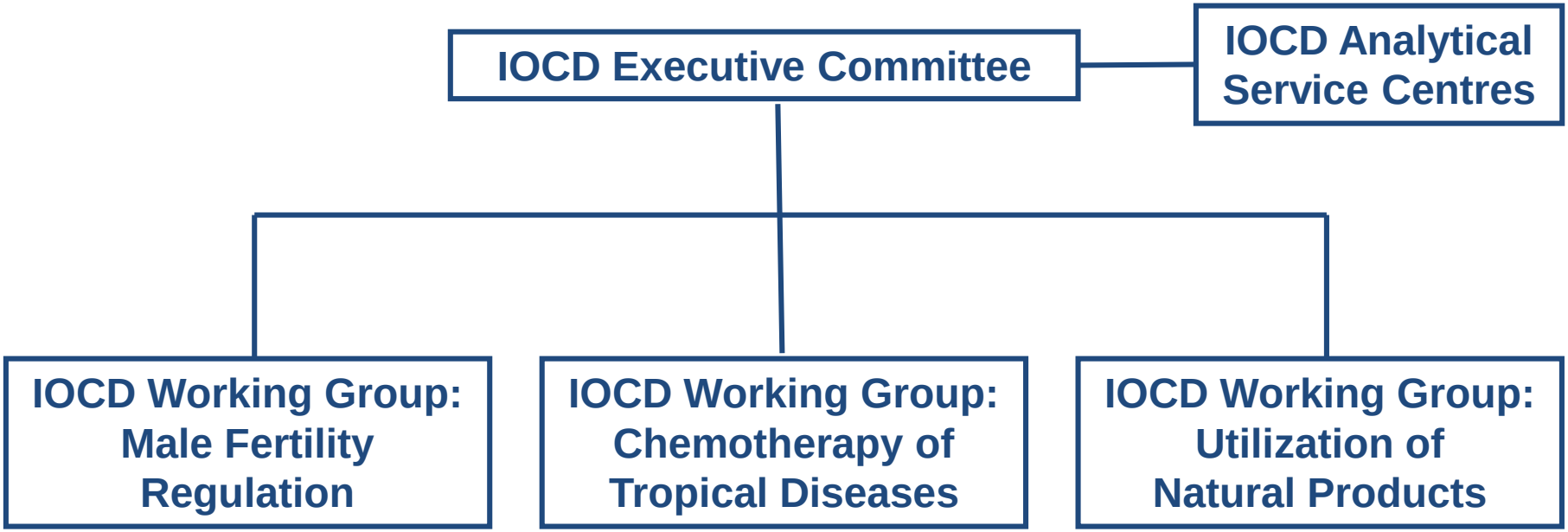


One does not go to a country to "assist" people, but to work with them in a new kind of endeavour. We should keep in mind that in cooperative programmes we learn more than we teach and receive more than we give.

International Organization for Chemical Sciences in Development

- belief in the vital role of science in aiding development
- deep concern about the barriers that hinder the research efforts of chemists in low- and middle-income countries (LMICs)

First phase 1981 - 1995



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First phase 1981 - 1995

- research projects
- research facilitation
- capacity building – mainly individual





March - April 1987, Oaxtepec, Mexico

- Large gathering of IOCD scientists
- Joint meeting with the WHO Task Force on Methods of Male Fertility

Robert Maybury **IOCD Executive Director 1987 - 2010**

Second phase 1995 – 2010

- **Less money**
- **New Working Groups & Projects**
- **Shift from research projects to meetings**

Robert Maybury **IOCD Executive Director**
1987 - 2010

Second phase 1995 – 2010

- **research facilitation**
- **capacity building – individual**
  institutions
  networks
  policy

IOCD Working Groups & Programmes 2010

1. Environmental Analytical Chemistry
2. Plant Chemistry
3. Biotic Exploration Fund
4. Tropical Diseases
5. Medicinal Chemistry
6. Books for International Development
7. Medicinal Chemistry: Open and Distance Learning
8. Organic Chemistry: Online Tutorials (Spanish)
9. Global Microscience Programme

Alain Krief **IOCD Executive Director 2010 -**

Third phase 2011 – 2020

- **World has changed**
- **IOCD must renew its strategy, methods and membership**
- **New Strategy 2011 – 2020**