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The French Technical Vaccination Committee (CTV)[☆]

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ABSTRACT

This article describes the make-up and activities of the Technical Vaccination Committee (CTV) that serves as the National Immunization Technical Advisory Group (NITAG) in France. Comprised of a variety of technical experts, the CTV makes recommendations concerning vaccination. The committee functions as an independent expert advisory committee, and its proceedings are confidential, although its recommendations are made public. It helps to make decisions about using new vaccines, as well as re-examining guidelines for vaccines already in use. It obtains technical expertise from a variety of sources, including specialized national centres. Although it is not obliged to do so, in most cases, the French government implements CTV recommendations. Information regarding CTV activities is disseminated through publications, its website, and letters to health officials. Efforts need to be enhanced in order to avoid creating a gap between the issuing of complex vaccination policies and their understanding by general practitioners who are responsible for the administration of over 80% of all vaccines.

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1. Description, background, and membership

The National Immunization Technical Advisory Group (NITAG) in France is known as the *Comité technique des vaccinations*, or the Technical Vaccination Committee (CTV). The CTV is comprised of 20 qualified members who represent a range of specialties pertaining to vaccination (Table 1). The CTV also has *ex-officio* members who represent agencies affiliated with the Ministry of Health, or other ministries and various institutions (Table 2).

While official legal documents on the establishment of the CTV and definition of its mission exist, there are no official written terms of reference for the committee. On the 27th of December 1985,

Table 1

 $Composition \ of the \ CTV: voting \ members.$

- Three specialists in infectious diseases
- Three pediatricians
- Two microbiologists
- Two specialists in epidemiology and public health
- Two general practitioners
- One immunologist
- One geriatrician
- One gynecologist-obstetrician/midwife
- One internist
- One maternal and child welfare physician
- One workplace physician
- \blacksquare One health economist
- One sociologist

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a ministerial order was made to set up the CTV as an independent expert advisory committee within the framework of the High Council of France for Public Hygiene (CSHPF). Several amendments were made to this first order, including the order of 12th November 1997 that describes in detail the CTV mission and membership. Prior to 1985, other similar entities had made recommendations on immunization. The oldest recommendation dates from 1822, when a plague epidemic in Marseille prompted the creation of High Council for Health. In February 1902, the first law relating to the protection of public health mentioned the creation of hygiene committees. The mission of the present CTV is defined by a ministerial order dated 18 September 2007 [1]. Its responsibilities include: evaluating scientific information on advances and perspectives in vaccination; developing vaccination strategies based on applicable

Abbreviations: ADIP, Accelerated Development and Introduction Plans; AFSS-APS, French Sanitary Safety Agency for Health Products; BEH, Epidemiology Weekly Bulletin; CEPS, Evaluation Committee of Health Products; CNAM, National Health Insurance Fund; CNOM, National Council of Medical Board; CSHPF, High Council of France for Public Hygiene; CSMT, Committee for Transmissible Diseases; CTV, Technical Vaccination Committee; DGS, General Directorate for Health; EURO, World Health Organization Regional Office for Europe; HAS, High Authority of Health; HCSP, High Council for Public Health; IGAS, General Inspection for Social Affairs; INPES, Prevention and Health Education National Institute; INVS, Sanitary Surveillance Institute; MA, market authorization; NITAG, National Immunization Technical Advisory Group; WHO, World Health Organization.

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Table 2 Composition of the CTV: *ex-officio* members.

- Two representatives of the Armed Forces Health Services
- The Director-General of the Direction Générale de la Santé (DGS)
- The Director-General of Social Services
- The Director-General of Education
- The Director-General of Social Security
- The Director of the Direction de la recherche, des études, de l'évaluation et des statistiques (DREES; the department responsible for oversight of research, studies, assessments and statistics)
- The Director-General of Employment
- The Director-General of the Agence française de sécurité sanitaire des produits de santé (AFSSAPS; the agency responsible for the assessment of health product safety)
- The Director-General of the Institut national de prévention et éducation à la santé (INPES; the institute responsible for implementing disease prevention and health education policy)
- The Director-General of the Institut de veille sanitaire (INVS; the institute responsible for health surveillance)
- The President of the *Conseil national de l'ordre des médecins* (the committee providing oversight for physician practice)

epidemiological data; conducting risk-benefit analyses (individual and population) and health economics studies on measures under consideration; and proposing changes to vaccine guidelines and making recommendations for immunization schedule updates.

As expressed in the 2004 public health law, "Vaccination policy is developed by the Minister of Health who establishes immunization conditions, sets forth necessary guidelines, and publishes immunization schedules after consultation with the Haut Conseil de la Santé Publique (High Council for Public Health or HCSP)" [2]. Vaccination guidelines are thus the responsibility of the government, which seeks advice from the HCSP, an authoritative public health advisory committee. This organization was established in 2006 as a successor to the Conseil Supérieur d'Hygiène Publique or the Superior Council for Public Hygiene [3]. The CTV was originally affiliated with the Commission de Sécurité Sanitaire (Health Security Commission of the HCSP) but is now attached to Commission des Maladies Transmissibles, or Committee for Transmissible Diseases (CSMT) of the HCSP.

The selection of CTV members is based on expertise. When there is a vacancy, the HCSP issues a call for experts on its website (www.hcsp.fr) and through its journal. After receiving letters of interest, a sub-committee is formed involving the General Directorate for Health (DGS), the French health authority of the Ministry of Health, to select members (via a closed process). Members of the CTV elect the Chairman. The duration of appointment for committee members is three years, which is renewable and the number of terms is unlimited. Members do not receive payment for serving on the CTV. Provided that the Chairman is not a member of the civil service (usually the case), the Chairman is remunerated for meetings over which he or she presides. Other members, for example the authors of reports, can be remunerated as well.

There are a number of *ex-officio* members who represent agencies affiliated with the Ministry of Health, or other ministries and various institutions. While they do not have voting power, they do have the right to participate actively in discussions. The information provided by two organizations, the INVS (*Institut de Veille Sanitaire* or the Sanitary Surveillance Institute) and the AFSSAPS (*Agence Française de Sécurité Sanitaire des Produits de Santé* or the French Sanitary Safety Agency for Health Products), often have a major impact on decision making. Usually, the texts are voted upon to reach consensus.

The committee is currently being evaluated by the *Inspection Générale des Affaires Sociales* (IGAS) or the General Inspection for

Social Affairs. This assessment may result in changes to the membership appointment structure in the next year.

2. Declaration of conflicts of interest and the conduct of meetings

2.1. Declaration of conflicts of interest

Routine reporting of any conflicts of interest regarding committee members is a requirement, and the management of conflicts of interest is a major concern. The CTV has a conflict of interest charter, which is coupled with a procedure to assess for conflicts of interest. Possible conflicts of interest must be declared annually, and these declarations must be kept up-to-date. At the start of each meeting, members must disclose any possible conflicts of interest they may have concerning topics on the agenda. The situation for each CTV member is analyzed before each plenary session by the Secretariat of the HCSP and possibly by the CTV Chairman as well. This also applies to members of CTV working groups.

Action is taken if a member has any apparent interests in relation to a vaccine or intervention to be discussed. The conflicts of interest charter consists of classification of potential conflicts of interest based on the AFSSAPS' classification of conflicts of interest [4]. If the conflict is classified as minor (e.g., a person was invited to a conference where industry paid registration fees and accommodation but provided no other benefits or compensation), this person may participate in debates and votes concerning the relevant topic. If conflict of interest concerning a particular topic is classified as major, the expert in question is excluded both from debates and votes pertaining to that topic. For example, an expert who is a coordinating investigator for clinical trials of a certain vaccine would be excluded from debates and votes concerning that vaccine, or competing vaccines or interventions.

2.2. Conduct of meetings

Members are not required to sign a confidentiality form or similar kinds of agreement. They are informed, however, that the content of any CTV proceeding is confidential. Despite the lack of formal agreements, the expectation of confidentiality is implicit and respected. The CTV has not yet had time to develop documents or guidelines as to what its members can disclose to the press.

CTV plenary meetings are held in the conference rooms of the Ministry of Health building, which also hosts the Secretariat of the HCSP. The plenary meetings of the CTV are not open to the public and are reserved for CTV members only. However, non-members may be invited to attend a particular presentation during the meeting. The CTV is expected to hold eight half-day meetings per year but in practice, eight meetings are not enough. Supplementary meetings are usually added, both on a scheduled program basis and *ad hoc* basis for exceptional circumstances. In 2008, the CTV held nine meetings. By the end of 2009, 13 CTV meetings were held, including four supplementary meetings that had not been previously scheduled.

The High Council for Public Health (HCSP) was originally created in order to separate medical expertise from the General Directorate for Health (DGS), and following this logic, the CTV became a part of HCSP. Initially, staff of the DGS' Office of Infectious Risks and Immunization Policy (the RI1 office: *Bureau Risque Infectieux* 1), along with the Secretariat of HCSP, was in charge of coordinating CTV meetings. This arrangement was changed in June 2009, and now, the Secretariat of the HCSP is entirely devoted to overseeing this task, with help provided by an executive secretary and assistant secretary. They prepare and coordinate the work and meetings of the CTV in collaboration with the Chairman. A core group is being

formed, including the Chairman, executive secretary, and two other committee members, which will be in charge of screening all referrals and deciding upon the next steps such as the formation of a working group. As the CTV is affiliated to the HCSP, it has no specific budget.

3. Scope of the CTV work and setting the agenda

The committee's work addresses several related topics within the scope of vaccines and immunization. Among them is decision making on the use of new vaccines (e.g., vaccinations against human papillomavirus (HPV) and meningococcus C are recommended, while universal vaccinations against chickenpox, rotavirus, and shingles are not). The committee also makes recommendations concerning vaccination schedules, as in a recent self-referral to the CTV to establish guidelines for the simplification of immunization schedules, as well as recommendations on vaccines for high-risk groups such as immuno-suppressed patients. It makes recommendations on vaccines for other vaccinepreventable diseases (e.g., re-examination of guidelines for use of the heptavalent pneumococcal conjugate vaccine, or defining the conditions of use for a pre-pandemic vaccine). Other recommendations concern vaccine formulations, such as the decision to not replace the trivalent MMR vaccine with the quadrivalent MMR-Varicella, as well as recommendations on the use of specific vaccines for the same disease such as the meningococcal B vaccine.

The CTV sets its agenda or program of work based on suggestions from various sources, including the DGS and pharmaceutical companies. The DGS refers any problems to the CTV that it identifies as being concerned with public health and vaccination. The companies inform the CTV when they are awarded marketing approval for a new vaccine or in the event of modification of a previous registration. The CTV can also decide to independently propose recommendations on issues that it thinks need consideration. However, this must be validated by an HCSP committee. To be considered for validation, a document must define the procedures and responsibilities for the working group (nomination of the chairman, membership make-up, functioning, production, and publication of guidelines), while another document outlines the procedures to be undertaken when a referral is received by the CTV, as well as an estimated timeline of expected deliverables.

Pharmaceutical companies may have a say in setting the agenda. As soon as a vaccine has obtained market authorization (MA), the owner of the MA can submit a dossier to the CTV in order to initiate the process of establishing guidelines on vaccine use. Granting the MA and establishing guidelines are separate procedures with different endpoints. The MA is granted by the AFSSAPS following an assessment of the efficacy and safety of the vaccine. Currently, registration procedures are European-based. Any possible guidelines for vaccine use are established after the MA is obtained, with the main criterion being the impact of the new product on public health. This type of procedure is not limited to new products; it may also be applied when new data on an existing vaccine show a change in its impact, thus affecting guidelines on its use.

4. Development of recommendations and basis for decision making

Sources of technical data and expertise available to the committee include official CTV members, national centres of expertise, invited *ad hoc* experts from within the country, WHO position statements, and working groups.

A referral made to the CTV concerning a particular topic usually leads to the creation of a dedicated working group that is responsible for investigating the topic. Separate working groups

are established to look at specific issues. The groups are *a priori ad hoc* but can be reactivated on as-needed basis (e.g., when reconsidering a recommendation based on new data). Certain groups (such as those concerned with meningococcus and influenza) are, in fact, permanent working groups due to their topical nature. There are no terms of reference for working groups.

When a referral is received, the CTV Chairman establishes a working group and proposes a working group chairman. The CTV Chairman then sends the chairman of the working group a *lettre de mission* or mission statement, which defines the fields of expertise needed, provides details on the delivery of the report, and may also propose a work plan. The working group chairman and the executive secretary select members of the working group, designate a rapporteur when needed, and establish the work schedule. Tasks are distributed among members according to their expertise or specialization. The rapporteur or chairman of the working group synthesizes the data collected by the members, develops the report, and drafts the recommendations. The Secretariat of the HCSP ensures that the necessary administrative functions are provided.

The recommendations developed by the working group are presented to the larger CTV. The committee assesses the working group's recommendations by discussing each of the recommendations and voting on them throughout multiple plenary meetings. Additional meetings may be held when an urgent health situation demands an immediate decision (for example, the recent publication of data suggesting a possible safety risk for children associated with the hepatitis B vaccine). In cases where experts disagree over adoption of a recommendation, they are settled by a majority vote. Usually, the preliminary discussions make it possible to obtain a very broad consensus or even unanimity. A slim majority vote or an elevated level of abstentions will result in further continuation of work. After an agreement is reached, CTV recommendations are then transmitted to the CSMT for validation. The CSMT is informed of the consensus level among the CTV members concerning the recommendations and may be requested to weigh in.

Working groups receive support on a systematic basis from: AFSSAPS on questions concerning vaccine safety; the *Institut National de Prévention et Éducation à la Santé* (INPES; the institute responsible for implementation of disease prevention and health education policy) on issues about communications policy; and the *Institut de Veille Sanitaire* (INVS; the institute responsible for epidemiological surveillance) for epidemiological issues. Currently, most CTV investigations consist of pharmaco-epidemiological studies, as well as disease modeling and assessing different vaccination strategies. This disease modeling component is a part of INVS' mission; INVS may carry out the modeling itself or assign it to a public health laboratory of its choice.

There is an opportunity for external members to participate, with some restrictions, in working groups or in the CTV's deliberations. External experts can be full members of a working group and may even chair it. They may also be invited to the CTV plenary meeting to present their reports (if they are chairman or rapporteur of the group) or to provide their expertise on a particular issue (for example, the National Reference Center may present its epidemiological findings concerning a pathogen). Industry experts cannot be members of a working group. However, a commercial company may be heard by the CTV at the request of the CTV or at its own request. In the case of health economics studies, the company may be asked to make a presentation to INVS.

The development of a recommendation by the working group takes into account technological advances associated with new vaccines, as well as the evolution of epidemiological characteristics of diseases in France and elsewhere. International guidelines (notably those from WHO) are considered, along with an assessment of the vaccine's risk-benefit ratio based on pharmaco-epidemiological

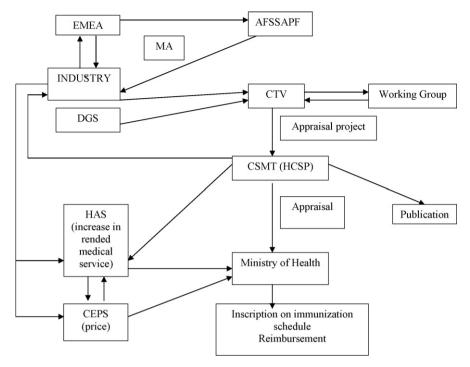


Fig. 1. Decision making process.

and modeling studies. Consideration of the organization of health and disease prevention systems is also an important element of the process. In the case of an alert of adverse events following immunization or of potential secondary effects, recommendations may include requests for strengthened vaccine safety surveillance. The primary vaccine-preventable outcomes that the CTV uses to generate recommendations are, in order of importance: overall morbidity, mortality, and hospitalizations, as well as epidemic potential. A referral from the DGS can include a request that outcomes be given extra consideration in the decision making process. Usually, however, the CTV assembles all of the information available in order to reach a decision.

Decision making by the CTV has not required that vaccine cost, overall program cost, affordability, and financial sustainability be considered. Even though the CTV has the authority to contract experts to conduct full economic analyses, it has not previously done so. However, economic studies have been taken into account for recent decisions (e.g., vaccines against rotavirus and HPV), and in the future, it is anticipated that most decision making processes will need to include an economic evaluation. Therefore, the CTV is having discussions with the HAS (Haute Autorité de Santé) on the content and format of these economic evaluations, and will put into place a working group to redefine the objectives and measures of the evaluations (at the moment, the INVS is in charge of economic evaluations and usually collaborates with a public health laboratory).

Economic analyses were taken into consideration during the formulation of recommendations for vaccinations against rotavirus, HPV, and meningococcus C. To reach those recommendations, a cost-benefit analysis was carried out using high and low price estimates of the vaccines. For the meningococcus C vaccine, the current price recommended by industry was considered high, while the price at which the government had purchased vaccines for previous vaccination campaigns was low. For the rotavirus vaccine, the chosen price for analysis was the current price recommended by industry. This raised a major issue since after recommendation of the vaccine is made, the vaccine price is negotiated between government and industry. Therefore, the changing price of the vaccine

means it probably should not be considered in the economic evaluation. This point is currently being discussed with the HAS. Economic analyses take a few months to complete, which delays decision making and prevents the CTV from fulfilling its time commitment to private companies. Economic analyses conducted in other countries can be taken into account but are not usually considered sufficient evidence upon which to base a decision. Economic studies undertaken by the pharmaceutical industry can also be taken into consideration but they are not considered sufficient. The current approach is to compare economic models during the period prior to reaching a decision.

5. Roles of the CTV and other key players in the decision making process

Once validated by the Committee for Transmissible Diseases (CSMT), the recommendations are published on the HCSP website and sent to the Minister of Health, who ultimately decides whether the CTV recommendations will be incorporated into the new vaccination schedule (Fig. 1). The vaccination schedules are updated annually and published in the official bulletin of the Ministry of Health. They are then published in the special annual issue of the *Bulletin Épidémiologique Hebdomadaire* (BEH; a weekly epidemiological bulletin published by INVS), the bulletin of the *Conseil National de l'Ordre des Médecins* (CNOM; the main professional organization for physicians), the bulletin of the *Comité d'Éducation Sanitaire et Sociale de la Pharmacie Française* (the Permanent Committee of the National Order of Pharmacists), the *Vidal* (French dictionary of pharmaceuticals), and other medical media, as well as in children's health textbooks.

When a vaccine has been recommended by CTV, the Commission for Transparency, which is a part of HAS, evaluates the impact of the administration of this vaccine on public health services (e.g., increase in rendered medical services). This evaluation will be used to determine the level of reimbursement (usually 65%) and will serve as a basis for negotiation of the vaccine's price between the vaccine manufacturer and the CEPS (Comité Economique des Produits de Santé or Health Products Evaluation Committee). Then the

government will decide whether or not the new recommendation will be integrated into the French immunization schedule.

The French government is not obliged to implement the CTV recommendations, although it has previously implemented most of them. Currently, vaccines recommended for the general population are subject to reimbursement. Some vaccines recommended for targeted use are not subject to reimbursement (e.g., hepatitis A vaccine for travellers or chickenpox vaccine for adolescents). The Ministry of Finance also plays a role in the decision making but the extent of its influence is unclear to many.

The Caisse Nationale d'Assurance Maladie (CNAM), or the National Health Insurance Fund, is a public-sector organization and is represented by ex-officio members of the CTV. The CNAM is a major player since it provides reimbursements for vaccines (seasonal flu vaccines, as well as vaccines against measles, mumps and rubella) but it does not interfere with the decision making process. Professional organizations generally do not play any role in the CTV decision making process, apart from the CNOM (Conseil National de l'Ordre des Médecins), the main professional organization for physicians that is represented by ex-officio members of the CTV.

Pharmaceutical companies do not play any financial role in the CTV decision making process even though representatives may be invited to make specific presentations at the discretion of the committee. Once a year, the CTV holds a specific meeting during which industry representatives are formally invited to present their activities; this allows the CTV to remain up-to-date about advances in the private sector. Special interest or lobbying groups do not provide any funding or other resources, nor do they intervene in the decision making process.

Two contrasting examples of decision making by the committee illustrate the gap between the committee's recommendations and the ultimate decisions that were put into place. The first example concerns HPV vaccination. The Ministry of Health and the media exerted pressure on the CTV by publicly announcing that there would be reimbursement of the HPV vaccine before the CTV issued its opinion. The difficulty in assessing the vaccine's cost-benefit status and target populations prompted the CTV to seek an economic evaluation and to decline on issuing its full recommendations by the requested date (rather, it issued limited recommendations concerning screening by cervical smear). Its final opinion was issued a few months later. However, media coverage of the HPV vaccine was very strong, and some people even considered it excessive. This subsequently led to vaccinations being overwhelmingly administered to the "catch-up" bracket group (women aged 15-23 years), with very little allocated to cover vaccinations for the targeted cohort group (girls under 14 years of age).

The other example concerns the meningococcus C vaccine, in which this case, there was no external pressure exerted on the CTV. The CTV reconsidered previous recommendations that were made on vaccination campaigns conducted in hyper-endemic areas. The epidemiological findings from the areas covered by the vaccination campaigns, which were compared with national data, played an important role in the decision making process. An economic evaluation resulted in the development of a vaccination strategy that is based on a single-dose immunization of one-year-old children, accompanied by a large "catch-up" effort for children, adolescents, and young adults. This was recommended in order to promote herd immunity, which can protect infants not targeted by vaccination.

6. Communications activities

In France, more than 80% of the vaccines are administered by mainly general practitioners (GPs), as well as private practitioners and pediatricians. Thus, a major issue lies in how to disseminate the recommendations and have them understood and accepted by physicians.

The CTV uses various tools for sharing information on CTV activities with the medical profession and the public. These include publications such as the *Guide des Vaccinations*, vaccination guides published by the INPES, medical professional meetings such as those held during European Immunization Week, and the websites of the HCSP and the Ministry of Health (a DGS site specific to vaccination is a work in progress). Other communications tools may also include letters from the committee to public health officials and physicians. Most CTV members are involved in training activities on immunization practices, even though this is not a part of CTV's mission.

The CTV's recommendations are made public, as well as the reports of its working groups. The validated recommendations are published on the HCSP website and in the special annual issue of the *Bulletin épidémiologique hebdomadaire* (BEH; a weekly epidemiological bulletin published by INVS). The minutes from the working group meetings and plenary meetings are not made public. In certain cases, a letter is sent to the DGS from the CTV Chairman but this letter is not made public either.

The vaccination schedule is published in several bulletins, such as the BEH, the CNOM and professional journals. Certain information on vaccines is also disseminated by CNAM, the National Health Insurance Fund. Finally, private companies are permitted to publicize their vaccines. The law no. 2009-879 of the 21st of July 2009 [5] states that companies are authorized to publicize their vaccines and that they must include a minimum number of sentences in all of their advertisements, which must be written by the CTV and validated by the HCSP and the AFSSAPS.

The CTV members communicate among themselves via meetings and e-mails. Working group members communicate via meetings or conference calls. The HCSP intranet portal, though active, is not currently used as a means of communication among CTV members. The CTV does not share information with other national expert committees.

7. Challenges, limitations, and future developments

Recently, the CTV and the HCSP had to deal with the influenza pandemic crisis. This experience has clearly demonstrated the credibility of their expertise and the impact of their recommendations. However, among the problems experienced by the CTV was a lack of funding since the scarcity of resources in the Secretariat also limits activities of the committee. Another problem was the lack of truly independent committee members, as it was virtually impossible to recruit members that were completely free from links with industry. However, this was balanced by employing strong, evidenced-based decision-making procedures, reducing the risk of influence and the associated loss of credibility. Finally, external expertise was hampered by the limited availability of influenza experts. During the current crisis linked to the pandemic flu, CTV experts have been and remain strongly committed to their home institutions, rendering them somewhat unavailable to examine the majority of issues addressed by the

The evidenced-based decision-making process of the committee could be further improved by clarifying the positions of the CTV and the HAS, especially when it comes to the conduct of economic evaluations. Additionally, it would be useful to clarify the positions of experts in relation to their original institutions, including the development of policy concerning their payment. Indeed, most members (including government officials) are not paid for their work with the CTV. This situation might be made more equitable if they could work officially for the CTV for a certain number of days per month and be reimbursed through their institutions by the DGS or the HCSP.

Some future changes to the committee are in the pipeline, and they include improving the understanding of vaccine guidelines, which are often unknown or misunderstood by health care professionals, despite numerous communications efforts using various means. In response to a DGS initiative, a strategic committee was formed to examine the issue of improving vaccination coverage. Other measures might be proposed, such as opening CTV plenary meetings to civil society or holding press conferences following the release of new and important recommendations.

8. Conclusion

As part of the deployment of the HCSP, the decision making process for vaccine-related recommendations was recently revised in France. Although the process may seem complex, its purpose is to guarantee high-quality, independent, and transparent expertise. The significance of the process was recently recognized by the WHO Regional Office for Europe (WHO EURO), since HCSP was asked to present about the CTV organization and its work at the WHO EURO meeting in Istanbul, Turkey in 2008 [6].

The current dilemma is how to avoid creating and widening the gap between the increasingly complex process of formulating vaccine policy and the implementation of that policy by general practitioners, for whom vaccination is not a primary issue despite the fact that they administer more than 80% of all vaccines in France. If a solution to this problem cannot be found, new immunization guidelines may not be translated into daily vaccination practice.

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Conflict of interest

DF has in the past received research grants from the Industry (Wyeth, GSK) and travel expenses for medical conferences by Sanofi Pasteur, Wyeth and GSK.

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