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Meeting report

Implementing efficient and sustainable collaboration between National Immunization Technical Advisory Groups: Report on the 3rd International Technical Meeting, Paris, France, 8–9 December 2014☆

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ABSTRACT

Many experts on vaccination are convinced that efforts should be made to encourage increased collaboration between National Immunization Technical Advisory Groups on immunization (NITAGs) worldwide. International meetings were held in Berlin, Germany, in 2010 and 2011, to discuss improvement of the methodologies for the development of evidence-based vaccination recommendations, recognizing the need for collaboration and/or sharing of resources in this effort. A third meeting was held in Paris, France, in December 2014, to consider the design of specific practical activities and an organizational structure to enable effective and sustained collaboration. The following conclusions were reached:

(i) The proposed collaboration needs a core functional structure and the establishment or strengthening of an international network of NITAGs.
(ii) Priority subjects for collaborative work are background information for recommendations, systematic reviews, mathematical models, health economic evaluations and establishment of common frameworks and methodologies for reviewing and grading the evidence.
(iii) The programme of collaborative work should begin with participation of a limited number of NITAGs which already have a high level of expertise. The amount of joint work could be increased progressively through practical activities and pragmatic examples. Due to similar priorities and already existing structures, this should be organized at regional or subregional level. For example, in the European Union a project is funded by the European Centre for Disease Prevention and Control (ECDC) with the aim to set up a network for improving data, methodology and resource sharing and thereby supporting NITAGs. Such regional networking activities should be carried out in collaboration with the World Health Organization (WHO).
(iv) A global steering committee should be set up to promote international exchange between regional networks and to increase the involvement of less experienced NITAGs. NITAGs already collaborate at the global level via the NITAG Resource Centre, a web-based platform developed by the Health Policy and Institutional Development Unit (WHO Collaborating Centre) of the Agence de Médecine Préventive (AMP-HPID). It would be appropriate to continue facilitating the coordination of this global network through the AMP-HPID NITAG Resource Centre.
(v) While sharing work products and experiences, each NITAG would retain responsibility for its own decision-making and country-specific recommendations.

1. Background

WHO establishes global vaccination policy recommendations but priorities may widely differ from one country to another, due to differences in the epidemiology of vaccine preventable diseases, and also to the level of national income [1,2]. An independent group of experts has become a standard basis for making recommendations concerning vaccination in public health policies at national level. Following the example of some countries with long-established experience, WHO encourages the creation of such National Immunization Technical Advisory Groups on Immunization (NITAGs) in all countries worldwide [3,4]. Currently, an effort is being made to ensure that all countries have sufficient support from NITAGs. To further advance this global effort, several groups of experts are working on the methodology and development of evidence-based recommendations in the field of vaccination policy in order to improve vaccination policy decision-making [5–9].

In November 2010, an international workshop was organized by the Robert Koch Institute in Berlin, Germany, with funding from the German Federal Ministry of Health, to discuss improved methods and harmonization of methodology for the development of evidence-based vaccination recommendations [10]. The

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objectives of the workshop were to review current procedures and experiences of NITAGs, discuss the applicability of methods such as *Grading of Recommendations Assessment, Development and Evaluation* (GRADE), and to identify opportunities for international collaboration to support NITAGs in the development of their country-specific vaccination recommendations. The participants concluded that (i) GRADE or a modification of this methodology is suitable for the grading of quality of evidence related to vaccine effectiveness and safety, and that (ii) international cooperation would facilitate the design of a common methodological framework for the development of national immunization recommendations in order to avoid duplication of efforts, build on existing strengths, and support NITAGs in all countries. Importantly, because vaccination decisions are not made in isolation but as part of a broader health sector policy, and policy on funding for vaccination varies in different countries, the relationship between NITAGs and their national health authorities needs to be examined and taken into account. As the characteristics and practices of NITAGs are heterogeneous, the potential of collaboration with other NITAGs may vary among countries. In an evaluation carried out in 28 European countries, 25 saw potential for such collaboration, but most often mentioned structural concerns due to differences in the organization of NITAGs and of countries' health care systems [11].

A second international workshop, also arranged by the Robert Koch Institute, was held in Berlin in September 2011 [12]. A broad international range of NITAGs and international organizations and expert groups were represented. The main conclusions were the following:

(i) In view of the work load involved in developing evidence-based vaccination recommendations, there is a need to share resources, results, and skills between the different countries.
(ii) Systematic reviews are the prerequisite for all evidence-based decisions and create the biggest workload for NITAG secretariats.
(iii) A common methodology such as GRADE would facilitate understanding of the decision-making processes of NITAGs, and the sharing of relevant documents (e.g. evidence tables, systematic reviews).
(iv) GRADE methodology is considered suitable to take into account relevant issues such as herd immunity, surrogate markers, passive disease surveillance, and post-marketing observational studies on vaccine effectiveness and rare adverse events following vaccination.
(v) Following the use of the GRADE system to establish the quality of evidence on vaccine effectiveness and safety, additional analyses of country-specific issues are required for the development of precise country-specific recommendations.

The first step, the evaluation of existing evidence on the effectiveness and safety of a vaccine, could be conducted in a collaborative international effort. In the second step, country-specific issues such as values, preferences, local epidemiology and disease burden as well as costs need to be considered individually by each NITAG. An international institution or working group (possibly at a regional level) is needed to coordinate these efforts and to identify minimum requirements for the preparation of relevant documents (such as systematic reviews) by each NITAG. As WHO regions are heterogeneous, the collaboration may start at a subregional level.

There was a general consensus at the Berlin workshops that collaboration would be the basis for progressing to an improved and harmonized methodology for the development of vaccination recommendations. Experts and/or authorities from several countries expressed willingness to take part in this collaboration.

2. Objectives of the 3rd international workshop

The main purpose of the third workshop was to move forward, based on the consensus reached in Berlin, to delineate working arrangements and priority activities. The first objective was to determine the content of the collaboration between NITAGs and their secretariats and its operational terms. The second objective was to define the institution or the network of institutions which could coordinate and facilitate this collaboration in the long term, i.e. a core functional structure and the establishment or the strengthening of an international network of NITAGs, possibly based on a series of regional networks.

Representatives of institutions involved in vaccination or public health policies were invited to give their opinions. In plenary sessions, following an overview of the two Berlin meetings, the participants reviewed the current issues, the identified needs and their possibilities for involvement in a common process. Workshops were organized to better define the tasks which could be shared and to agree on a chart of inter-NITAG collaboration. The main recommendations and conclusions reached during the meeting are presented below.

3. Formalizing the networking of the NITAGs

Two levels of collaboration were identified: (i) collaboration to systematically exchange and share final "work products" widely via a joint platform, and (ii) collaboration to jointly develop or commission "products" such as systematic reviews, generic disease transmission models, studies, protocols, publications, etc. It is necessary to identify a host institution (or institutions) for coordination and management, and a funding source for both of these levels of collaboration. While the first level of collaboration can be achieved at global level, the enhanced collaboration (second level) seems more feasible if organized at regional or subregional level based on existing infrastructures and involving NITAGs with similar priorities. Particularly for the enhanced collaboration, a code of conduct would have to be agreed upon to govern the sharing of unpublished results, and working procedures defined. Each NITAG that is part of the network should continue its activities but the sharing of information should be facilitated. It may be possible to begin with a pilot mechanism that could be adapted and improved with experience. It is also necessary to set out the main objectives and outputs for each participating structure.

Expansion of the network will be important, bringing in more countries with broader geographic representation, including countries with limited resources and experience in this domain, with the ultimate aim of creating a global NITAG collaborative network, possibly based on a series of regional networks. NITAGs already collaborate at the global level via the NITAG Resource Centre, a web-based platform developed by the Health Policy and Institutional Development Unit (WHO Collaborating Centre) of the Agence de Médecine Préventive (AMP-HPID). It would be appropriate to continue facilitating the coordination of this global network through the AMP-HPID NITAG Resource Centre [13]. Since in the European Union (EU) there are already advanced discussions on a regional network to support NITAG work, the following section will focus on the EU. In other regions, similar activities could be carried out.

4. The possible role of existing international institutions in Europe

4.1. European Centre for Disease Prevention and Control

A work package of the ECDC-funded "Vaccine European New Integrated Collaboration Effort" (VENICE) III project has as its aim

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the development of a roadmap for better sharing of data, resource and methods between NITAGs in the EU. A 5-country core group met in Berlin in November 2014 to develop the draft roadmap for the process. The roadmap will be shared with all EU member states before validation by ECDC.

There are potential areas for collaboration between ECDC and the NITAGs, especially since many NITAGs are supported by executive secretariats that are hosted by National Public Health Institutes. Potential areas for collaboration include the sharing of best practices and knowledge across member states, notably best practices in the assessment of disease burden, the application of evidence-based public health methodologies, or the conduct of mathematical modelling and cost-effectiveness analyses before the introduction of a new vaccine. ECDC can provide scientific, evidence-based information and guidance, and support the exchange between National Public Health Institutes, but its mandate does not include the development of vaccination policy recommendations for countries.

4.2. The European Commission

In principle the European Commission may promote information sharing among member states to facilitate coordination, especially in relation to options for actions through guidelines and preparation of necessary elements for regular monitoring and evaluation. Regarding the collaboration between NITAGs, the Commission is currently exploring possibilities to support member states in these efforts. Use of the Health Programme (2014–2020) as well as other EU instruments to support specific areas that can be of added value in strengthening vaccination at EU level should be explored.

The European network for Health Technology Assessment (EUnetHTA) has recently expressed its interest in including NITAG collaboration in its terms of reference. This network is mainly funded by the European Commission. The question was raised as to whether EUnetHTA could be used as a platform for a sustainable system of knowledge sharing and promoting good practice in methods and processes.

4.3. The Council of Europe

Recently, the Council of Europe issued a position statement on vaccination as an effective tool in public health. This statement is aimed at placing renewed emphasis on vaccination in the EU public health agenda and highlighting the need for strengthened cooperation.

There is a call for greater collaboration between the European organizations. Both WHO and the EU would be able to contribute financially to support this effort. The work of the EU would complement the recently released WHO European Vaccine Action Plan 2015–2020.

5. Discussion on technical aspects of the collaboration

5.1. Scope of collaboration

A list of proposed topics for collaboration emerged from the Berlin workshops. During the Paris meeting, some experts considered that it would be preferable to start by selecting two or three topics for further work initially. However others preferred to retain the full list of potential collaboration topics from which each NITAG could select according to its experience and priorities.

At the Paris meeting, topics selected as priorities for inter-NITAG collaboration included: systematic reviews, background to NITAG decisions, and cost-effectiveness analyses. For collaboration on systematic reviews, a list of subjects will need to be agreed. Collaboration for the background to a NITAG decision would not be necessary for all recommendations but would be crucial for important questions such as the decision to withdraw a vaccine, or to introduce a new vaccine. Regarding cost-effectiveness analyses, health economics may be considered as specific to individual countries, but generic models can be developed in a collaborative effort or jointly commissioned, for instance an academic institution, and then later adapted to each participating country's setting.

Other topics were also considered important, such as disease transmission models, evaluation of the burden of disease, and the acceptability of vaccines by the population. NITAGs should also play a role in encouraging the production of good quality data. Depending on the epidemiological situation and countries' priorities/resources, some of the topics would have regional rather than global relevance.

5.2. Methodology

As well as the topics for collaboration, there needs to be agreement on the methodologies to be used. For example, quality appraisal tools and a system to grade the quality of the body of evidence should also be applied when conducting systematic reviews, to guarantee a high standard and transparency which are necessary for other NITAGs to be able to trust and reproduce the work. Systematic reviews could be embarked on immediately, allowing the process to start and gather momentum. Sharing the background to the recommendations would be relatively simple, requiring only a platform for exchanges to be set up.

AMP-HPID commissioned a study, conducted in collaboration with the Dutch NITAG, to review the topics of the recommendations issued from 2011 to 2014 by five well-established European NITAGs, in order to identify the common topics and therefore assess the level of collaboration that can be envisaged among European countries. VENICE has carried out a survey of collaboration concerning meningococcal B vaccination. Similar work should be carried out in other regions to provide a global picture of the possibilities for information sharing and collaboration. Regarding the methodologies to be applied, GRADE and other assessment tools should be promoted.

5.3. Information sharing

Sharing of information could take place at two different levels: (i) the sharing of work and results that have already been completed and (ii) the carrying out of joint work by two or more NITAGs. It is necessary to move faster on certain topics, notably the models of structure and the standard operating procedures. Transparency is a key component for collaboration, and this involves sharing processes, agendas and work plans. Information is sometimes obtained from academic groups and industry and some may be reluctant to share data before publication. Confidentiality and trust emerge as the most important factors for successful collaboration. Building trust will be a beneficial output of the collaboration.

Ownership issues for non-published final products should be addressed. The point arises primarily in cases where information is shared in confidence between NITAGs or NITAG secretariats. Agreements would have to be negotiated before any collaboration begins. A contractual relationship is necessary (e.g. a Memorandum of Understanding). This could be shared with other NITAGs in a tri-partite agreement. Confidentially agreements should probably also apply to liaison members. Ensuring that conflicts of interest are fully declared is also essential. A list of NITAG products that could be shared should be decided: meeting reports, confidential minutes, press reports, commissioned reports, and systematic reviews

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etc. A question to be resolved is whether commissioned products involving other agencies should be shared.

In addition to sharing final products, NITAGs should be involved in other activities such as training, twinning of NITAGs (mainly at the regional level), sharing of generic protocols or generic models, and the creation of a resource directory. Providing assistance, including training, for recently formed NITAGs is an important priority. As soon as the relevant legal structure has been set up, questions of methodology become a top priority. Literature reviews are another area of interest for recently-formed NITAGs.

An agreement was reached for the following topics as highest priorities for collaboration and information exchange: (i) systematic reviews, (ii) policy documents that justify a decision, and (iii) modalities of functioning, which are of particular interest for recently-formed NITAGs. The issues and challenges associated with sharing information are relatively minor and could be resolved. Once collaboration is underway, any emerging challenges can be addressed in a second step.

6. Choice of institutions and modalities of collaboration

With global collaboration as the final goal, it was agreed that enhanced regional collaboration should be the focus initially, upon which the broader NITAG network, or a series of regional networks, could be developed. In the EU, collaborative arrangements already exist under the leadership of ECDC which can serve as a starting point for a regional or subregional activity. In other regions, similar networks or activities can be established.

The European network for Health Technology Assessment (EUnetHTA) was established to create an effective and sustainable network for health technology assessments (HTAs) across Europe and is already operational. This network facilitates common work to help in developing reliable, timely, transparent and transferable information to contribute to HTAs in European countries. It was agreed that EUnetHTA was not appropriate as a regional host institution because its objectives and methodologies differ from those proposed for the NITAG network.

As a WHO Collaborating Centre, the AMP-HPID, Paris, France, which hosts the Supporting Independent Immunization and Vaccine Advisory Committees (SIVAC) Initiative, was proposed as an institution which could potentially host the secretariat of the global network. The activities should include collaboration between well-established NITAGs that work in a similar manner, and collaboration between recently established NITAGs and more mature organizations. Regardless of their stage of development, all NITAGs would benefit from this work. Existing WHO models and structures could be reinforced and expanded to other parties. For Europe, a regional steering committee under the double umbrella of WHO and ECDC could be used to liaise with other partners and facilitate the work. Appointment of a responsible person to pilot this work is necessary, and for network coordination, a dedicated team (at least one expert and some with internet technology expertise) will be needed; it will be essential to build up the capacity of the Secretariat.

This experience could develop step by step, starting in the EU, then expanding to the WHO European Region (WHO-EURO) and to other WHO Regions. A communications platform is essential and the NITAG Resource Centre (NRC), developed by the WHO Collaborative Centre and partners, was proposed for this function. This NRC is not only a SIVAC mechanism but also a collaborative platform involving WHO, the US-CDC, Gavi, the Bill and Melinda Gates Foundation and others. A recommendation was agreed to build on this platform, ensuring that it is dynamic and adapted to the needs. An evaluation will be needed at a later point. Current funding of the NRC is available until the end of 2017.

As there will be no additional funding from the EU in 2016 for AMP-HPID, arrangements should be made to set up a self-funded network, with co-financing of the collaboration by the countries involved. Low and middle income countries should contribute by providing data, time and expertise. Funding is needed to support a secretariat. Countries which can do so should pay for their NITAG chairpersons to travel for training and information-sharing purposes. The preferred scenario to emerge from discussions is a regional coordination for technical activities, with global oversight and coordination for the information sharing processes. The platform could be used to define objectives and a work plan.

7. The role of VENICE/ECDC in the NITAG collaboration

It was considered that VENICE could closely collaborate with NITAGs at European and global levels. This could be arranged under the coordination of ECDC, as VENICE is an ECDC-funded network. Discussions between European NITAGs and/or National Public Health Institutes on their potential collaboration have already started under the auspices of ECDC/VENICE. Countries outside the EU should not necessarily be included under the umbrella of the countries within the EU. However, there should be a mode of interaction between the EU-network with other regional activities or NITAGs outside the EU. Depending on the level of collaboration, this would also require the development of a code of conduct.

There is no overlap between collaboration among the NITAGs and the work of VENICE. The purpose of VENICE is to function as a broader, more technical network (involving, depending on the country, the NITAG executive secretariat, National Public Health Institute and/or the NITAG directly) that provides support to NITAGs in their work. It is concerned with the development of common tools and jointly carrying out the work that NITAGs can use as a basis for decision-making (e.g. joint conduct of systematic reviews or development of generic transmission models). VENICE could not become a network of all NITAGs, because ECDC just works only with countries of the EU and of the European Economic Area. AMP-HPID will explore the possibility of having in each region and country a focal entry point to the NRC and take steps to ensure that the arrangement works in practice.

8. The network around the NITAG Resource Centre (NRC)

The NITAG network should progressively expand, bringing increasing numbers of less experienced NITAGs into the system. The network will therefore include NITAGs that produce more information, and others which, initially at least, produce less. The terms of reference for collaboration in the network should therefore be discussed by each region, taking into account the important role played by the regional technical advisory group. Translation of documents among regions may be a constraint and is not always possible. However AMP-HPID is already acting as a bridge between regions and has dedicated budget lines for translation.

Participation in the network should be voluntary, but with a minimum set of obligations and commitments. Two key factors for success were identified: participation should be complete and the pitfall of duplication should be avoided. Collaboration requires the building of capacity and strength of the committees and some training will be needed. National governments will not necessarily take on board comments and recommendations made by the regional NITAGs.

The existing ECDC platform is an important resource and should be linked to and feed into the resource centre where appropriate. As NITAGs are not always aware of where to send material, AMP-HPID should write to each NITAG secretariat and ask for material to be posted to the site. It is important that the relevant products be available for the benefit of all countries. For countries with less

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experienced NITAGs, the priority is to have access to the work done by the more mature NITAGs: in order to make best use of that work, they will need training in the form of workshops. The concept of fairness was raised, noting that the same country should not always contribute to the generation of work products such as systematic reviews. The criteria for proactive advocacy and transparency should be defined.

9. Different types of collaboration at different levels

The regional collaboration on products has to be continued. At the global level, NITAGs already collaborate via the AMP-HPID platform, and collaboration to develop the products should be reinforced among core countries. An overall global effort, together with specific region-based initiatives can be implemented; for instance, not all countries would take part in joint work on systematic reviews. The collaboration should begin on a small scale, going forward step by step, starting with simple actions that would help build a positive momentum. As an example, AMP-HPID could consult with the most experienced NITAGs to decide on which information should be included and which information should be restricted to NITAG members.

10. Conclusions and next steps

This 3rd workshop demonstrated a shared willingness to participate in the proposed global NITAG network. Priority topics for collaborative work are systematic reviews, background information for recommendations, generic mathematic and health economic models, and establishment of common frameworks and methodologies.

The collaboration should begin with a limited number of NITAGs that already have a high level of expertise. While at global level the exchange of final products and experiences should be promoted, a more enhanced collaboration can be established in regional networks.

For the EU region, concrete activities should be launched under the auspices of ECDC/VENICE in collaboration with WHO. A road map for better collaboration is being developed by the VENICE consortium and will be submitted to ECDC. It was proposed that a EU stakeholder meeting should be held, at which EU member states and ECDC could agree on a structure, mode of collaboration and the required resources.

The ECDC area of interest may cover EU countries for limited activities, such as the funding of workshops or training, but not for long term projects, and ECDC cannot directly provide support to non-EU NITAGs.

A global steering committee for the NITAG network should be set up to support the interchange between regional or subregional networks.

The amount of joint work should be increased progressively through practical activities and pragmatic examples. It should be possible for many countries to fund their involvement in collaborative activities. The AMP-HPID NRC should host this experience with AMP-HPID having a greater role in the future. Regional networks such as VENICE/ECDC could contribute with final products in this collaboration. It is important that a broad range of NITAGs contribute to the NRC, as the level of heterogeneity is great, even within regions. Translation is a constraint, and the possibility of assistance from WHO and AMP-HPID will be explored.

Next steps will be organized after discussions between WHO, AMP and VENICE/ECDC.

Following the Paris meeting:

- a new version of the NRC was launched in March 2015 and is proactively tracing all types of documents identified by the group during the meeting and will make them available without restriction to all NITAGs. It provides a global database of NITAG-related documents, recommendations, tools, guidance documents, contact details for all NITAGs worldwide, as well as WHO vaccine recommendations. The terms of reference of this platform will be written and shared with partners, and a global steering committee will be established to supervise its activities.
- a VENICE III expert meeting was held in Berlin, Germany the 2–3 December 2015, where participants agreed on the strengthening of collaboration between NITAGs within the EU, starting with countries which would volunteer to take part.

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