Safety in administering medicines for neglected tropical diseases

Web Annex A. Training modules for programme managers
Module 1: Introduction

1. Welcome

Welcome to a series of WHO training modules on safety to accompany the main document. These modules are intended to help national programmes for neglected tropical diseases (NTDs) plan, prepare and monitor the safe administration of medicines for treatment of these diseases. This guidance consolidates and underscores recommendations on safety from existing WHO guidelines and documents; it does not make new recommendations.

2. Intended audience

This series of training modules is intended for NTD programme managers, national and subnational public health workers, community drug distributors and community health workers, WHO regional and country office staff, nongovernmental organizations and other implementing partners, and donors that support control and elimination of NTDs. This module introduces the topic of NTD safety and provides an overview of the other modules in the series.

3. Learning objectives

The learning objectives for this module are to:

- become familiar with the global “patient safety” movement and its importance for NTD programming;
- be familiar with the challenges to safety in administering medicines for NTDs; and
- understand the definitions of adverse event and serious adverse event, and the types of adverse events that should be investigated and reported.

4. Safety in global health

Global health programmes have two primary ethical responsibilities: to deliver health benefits to populations and – equally importantly – to prevent harm to individuals. Reflecting both of these responsibilities, WHO, in its Thirteenth General Programme of Work, 2019–2023, established an ambitious goal of universal health coverage, which requires the availability of safe, effective and affordable essential medicines and their correct administration and use. The cross-cutting targets of the NTD road map for 2021–2030 align with this goal through the promotion of high-quality, safe,
people-centred interventions against NTDs, including individual case-based treatment as well as mass drug administration (MDA), also called preventive chemotherapy.

Safety is crucial for the success of global health programmes. In 2019, the World Health Assembly adopted resolution WHA72.6 on global action on patient safety, urging Member States to “promote a safety culture” and requesting WHO to develop “normative guidance on minimum standards, policies, best practice and tools for patient safety” and provide support to Member States in training and building technical capacity to assess, measure and improve patient safety.

5. **Safety in NTD programmes**

Safety has long been a concern for NTD programmes, and it is increasingly important, as NTD programmes now reach more than one billion people each year. Attention to safety is required at every step of the process. The medicines that are donated for treatment and prevention of NTDs are manufactured under stringent regulatory guidelines or prequalified by WHO. Before WHO approves the co-administration of medicines for treatment of multiple NTDs, such as ivermectin, diethylcarbamazine and albendazole for lymphatic filariasis, intensified surveillance for adverse reactions is required in thousands of people. Considerable effort goes into maintaining safety throughout the supply chain, and WHO has issued practical advice for national programme managers on the prevention, detection and management of serious adverse events during preventive chemotherapy.

6. **Treatment-related adverse events**

Despite these substantial efforts, adverse events related to medicines do occur.

These adverse events have several different causes. Some are related to the pharmacological properties of the medicine and are known as “side-effects”. Most of the side-effects of NTD medicines are transient, self-limiting and mild in severity. However, some of the medicines used for individual case management of NTDs, such as melarsoprol for human African trypanosomiasis or liposomal amphotericin B for visceral leishmaniasis, are associated with significant side-effects and toxicity. For these patients, treatment must be carefully administered in a clinical setting and monitored for safety. Safety and toxicity of snakebite antivenoms are also a concern.

With MDA, most adverse events are related to the action of the medicine against the infectious organism being targeted, rather than to the medicine itself. For example, people with lymphatic filariasis who are treated with antifilarials commonly experience transient fever, myalgias and headache; such reactions are expected, transient and easily managed. Adverse reactions can also result from the action of the medicine against organisms that are not specifically targeted by MDA. For example, people with Loa loa infection who receive ivermectin for onchocerciasis control are at risk of encephalopathy.
Adverse events can also be related to how the medication is administered. For example, young children have fatally choked on deworming tablets. Available evidence, although limited, suggests that forcing children to swallow tablets against their will is the main risk factor for choking.

7. **Serious adverse events**

A small proportion of adverse reactions are classified as serious. A “serious adverse event” is a regulatory term describing a medical event that is fatal, life-threatening, disabling, results in hospitalization or in congenital anomaly or birth defect after intake of medication.

8. **Adverse events that should be investigated and reported**

Serious adverse events can threaten NTD programmes by reducing community confidence and trust. So prompt investigation, management and reporting is important, not only for serious adverse events but also for clusters of cases, which affect groups of people, and any adverse event that causes significant community concern or disruption, particularly where the cause is unexplained or “operational error” is suspected. Additional detail on identifying, investigating and reporting adverse events is provided in module 5.

9. **Challenges to safety**

Maintaining safety in NTD programmes requires continued vigilance. In addition to serious adverse events, other threats to programme safety include incomplete reporting and investigation of serious adverse events; inadequate coordination with national pharmacovigilance programmes; lack of safety training for community drug distributors; and challenges to clear, effective risk communication with stakeholders, including communities and the mass media.

10. **Culture of safety**

In the spirit of WHA72.6 and the NTD road map, programmes should foster a “culture of safety” and adopt a continuous cycle of assessing current practices and attending to individual and systemic factors associated with gaps in safety. Safety should be embedded in, and permeate, all aspects of NTD programmes, including training; supervision; medicine supply and management; individual treatment and preventive chemotherapy; communication with communities; programme monitoring; and prompt investigation and reporting of serious adverse events. Ideally, safety-related goals, objectives and activities should be articulated in national NTD master plans.

11. **Modules in this series**

The modules in this series address key areas for improving safety. They are intended for NTD programme managers and others. A companion series has been prepared for community drug distributors (Annex 3).
• Module 2 addresses safe management of medications, including procurement, shipping and storage, formulation and administration.
• Module 3 addresses prevention of choking.
• Module 4 provides the rationale and suggestions for greater collaboration with national pharmacovigilance agencies to improve NTD programme safety.
• Module 5 addresses the identification, management and reporting of adverse events.
• Module 6 provides guidance on communications to improve NTD programme safety and effectiveness.

Thank you for your attention.

Remember: you can make a difference in creating a culture of safety for control and elimination of NTDs.
Module 2: Safe management of medicines

1. **Welcome**

Welcome back to our series of WHO training modules to accompany the guidance document. These modules are intended to help national programmes for neglected tropical diseases (NTDs) plan, prepare and monitor the safe administration of medicines for treatment of these diseases. This module addresses safe management of medicines.

2. **Learning objectives**

The learning objectives for this module are to:

- understand how the safety of medicines and their administration are integral to NTD programmes, from manufacture to administration;
- understand what is meant by “age-appropriate formulation” of medicine and why it is important for NTD programmes;
- be familiar with exclusion criteria for preventive chemotherapy and their rationale; and
- understand the role of drug administration in ensuring safety of NTD programmes.

3. **Overview**

Safety in NTD medicines involves several important steps, beginning with the manufacture of high-quality medicines that are proven safe and effective; their licensing by regulatory agencies or prequalification by WHO; the formulation of these medicines so that they can be safely taken by people of different ages; supply chain, involving international shipping, local transport, and proper storage and management of stocks; and, finally, safe administration at the point of use.

4. **Manufacture**

Safety begins with the development and testing of high-quality medicines that are manufactured according to product specifications that comply with stringent regulatory authority guidelines or to criteria for prequalification established by WHO. Prequalification is a process overseen by WHO that facilitates access to quality-assured medicines and vaccines. To date, five essential medicines
have been prequalified by WHO for treatment of NTDs: ivermectin, mebendazole, praziquantel, diethylcarbamazine, and fexinidazole.

5. **Quality assurance**

Pharmaceutical companies currently donate medicines for treatment of 13 NTDs. These medicines are manufactured to high-quality standards under stringent regulatory authorities. Whenever possible, programmes should use medicines that are licensed by a stringent regulatory authority or that have been prequalified by WHO. For NTD treatment that relies on other generic medications, the quality, safety and effectiveness of available medicines can be a source of concern. The medicines donated for use against NTDs are shown in Table 1 of the accompanying guidance document.

6. **Drug formulation**

Safety also depends on the formulation of the medicine. Very young children and elderly people typically have difficulty swallowing large tablets, which sometimes leads to choking. Particularly in mass treatment settings when medicine is being given to large numbers of healthy children, age-appropriate formulations are an essential safety feature. Depending on the size of the tablet and the conditions under which it is administered, the risk of choking is highest for children aged under 3 years; it declines above this age but is never zero.

7. **Age-appropriate formulations**

Age-appropriate formulations for younger children include liquid preparations (e.g. oral suspension), granules and dispersible formulations. Azithromycin is available in an oral suspension for treatment of trachoma, and mebendazole is available in a dispersible tablet. An age-appropriate formulation of praziquantel is in development.

For deworming medicine (albendazole or mebendazole), WHO recommends that tablets be crushed before giving them to young children, even if they are considered “chewable”. Crushing tablets is not currently recommended for treatment of other NTDs during MDA (e.g. azithromycin for yaws), partly because of lack of evidence that crushed tablets provide equivalent pharmacological benefit. Additional information on formulations of medicines and prevention of choking is provided in module 3 of this series.

8. **Shipping and storage**

The safety and quality of medicines used in NTD control programmes also depend on how they are shipped and transported from the point of manufacture to the person taking the medicine, as well as on secure storage and recommended stock management in the central and district medical stores. WHO, working in collaboration with the NTD Supply Chain Forum, has developed standard operating protocols and procedures to ensure safe, secure transport and storage of NTD medicines. Both the safety and the potency of the medicines require that they are stored under recommended conditions of temperature and humidity. For medicines used in preventive chemotherapy, the NTD Supply Chain Forum has also issued guidelines for management of inventory to minimize
loss, damage, contamination and misuse, and to avoid expiration of medicine. The “first-in-first-out” principle of inventory management should be followed. The WHO Joint Application Package helps national programme managers to coordinate requests for multiple NTD medicines, as well as organize their safe transport, storage and use. For azithromycin used in trachoma control, these topics are covered in the Zithromax management guide published by the International Trachoma Initiative in 2019. Programme managers should be familiar with these important resources.

9. Administration

Even with medications that are pharmacologically safe, available in age-appropriate formulations and that have been appropriately shipped and stored, proper administration at the “point of use” is essential for safety. It is at the point of use that mistakes and operator errors most frequently occur. Safety can be enhanced by giving careful attention to key aspects of drug administration. These include: inspecting medicines in advance to ensure that they are in good condition (e.g. tablets not broken or disintegrated) and have not reached the expiry date; arranging the environment to minimize confusion; adhering to recommended exclusion criteria; clear labelling and use of appropriate containers if re-packaging is necessary; proper dosing; restricting co-administration of medicines to WHO-approved combinations; and attention to infection control.

10. Safe setting or environment

Studies in hospital settings document that operator error occurs frequently. Operator error is a significant reason for improper dosing, administration of the wrong medicines and lack of attention to safety. Risk factors include ambiguous instructions or policies, fatigue, confusion, noise and other distractions. These risk factors undoubtedly contribute to error during treatment with NTD medicines, whether in individual or mass treatment settings.

NTD programme managers can encourage community drug distributors to carefully organize their work environment, pay attention to crowd control and recruit enough assistants to allow for the smooth flow of MDA.

11. Exclusion criteria in preventive chemotherapy

Even though the medicines used in preventive chemotherapy are pharmacologically safe, excluding certain people is a crucially important safety measure. Individuals with serious illness should be excluded from preventive chemotherapy because they are more likely to experience adverse health events in general (related to their illness, not to medicine ingestion) and because any medicine-related adverse events they experience are more likely to be serious. Seriously ill individuals are defined as those who:

• have an illness that makes them too sick or weak to get out of bed; or
• are currently hospitalized.

Additional general exclusion criteria include:

• age (the lower eligible age varies for different medicines);
• pregnant women (with exceptions);
• people diagnosed with neurocysticercosis or a history of seizures or epilepsy;
• individuals who have previously suffered from serious adverse events caused by a reaction to the medicine, such as Stevens–Johnson syndrome.

Additional information is provided in the next slides on exclusion for age, pregnancy and symptoms of neurocysticercosis.

11.1 Age

The medicines used in mass drug treatment all include young age as an exclusion criteria, but age of eligibility differs. Special attention to age criteria is warranted when co-administering several drugs during MDA. The exclusion criteria for preventive chemotherapy in young age are given in Table 3 of the accompanying manual.

11.2 Pregnancy

Evidence varies on the risk of different NTD medicines during pregnancy. Although studies in humans have not found a statistically significant increase in the occurrence of congenital anomalies or adverse birth outcomes after women were inadvertently exposed to the medicines currently used in preventive chemotherapy, in general, women in the first trimester of pregnancy should be excluded from MDA.

During the second and third trimesters, WHO recommends excluding women from MDA with ivermectin or diethylcarbamazine out of an abundance of caution. Conversely, for women living in areas where soil-transmitted helminthiases are endemic, particularly hookworm infection, WHO recommends deworming during the second and third trimester of pregnancy. WHO also recommends that pregnant women in the second or third trimester not be excluded from mass treatment with praziquantel or azithromycin. The exclusion criteria for pregnancy and lactation are given in Table 4 of the accompanying manual.

11.3 Neurocysticercosis

A Guideline Development Group at the Pan American Health Organization has drafted recommendations for preventive chemotherapy for control of taeniasis and neurocysticercosis. This guideline recommends preventive chemotherapy with periodic single-dose niclosamide or praziquantel or, if those medicines are not available, three daily doses of albendazole (for persons > 30 kg in weight) for control of taeniasis.

During preventive chemotherapy with albendazole or praziquantel, whether for taeniasis or other diseases such as schistosomiasis or soil-transmitted helminthiases, people with symptoms compatible with neurocysticercosis (i.e. a history of intense or severe and progressive headache, or of epilepsy or seizures of unknown cause), or with subcutaneous cysticercosis, should be excluded.

11.4 Treatment of NTDs not suitable for preventive chemotherapy
When treatment of NTDs occurs in a clinic or medical setting, there may be precautions or contraindications to treatment with recommended drugs. As with other treatment in medical settings, the clinician must weigh several considerations including progression of disease in the absence of treatment, risk of adverse reactions, interactions with other drugs the patient is taking, and alternative courses of treatment.

12. **Packaging and re-packaging**

Medicines that are donated by research-based pharmaceutical companies for control of NTDs and those that are prequalified by WHO are packaged to ensure integrity, potency and safety as long as they are stored under recommended conditions. As much as possible, medicines should be kept in their original, clearly-labelled containers until they are administered. However, medicines for MDA, in particular, are often provided in bottles with hundreds of tablets. NTD programmes may find it necessary to re-package these medicines in smaller quantities when preparing for MDA in remote communities. Such re-packaging presents opportunities for errors and confusion. Programme managers should be aware that as soon as a bottle of tablets is opened, the expiration date for the medicine may be compromised and the potency of the tablets cannot be guaranteed.

However, if re-packaging is necessary, the containers used for re-packaging should be clean, durable and labelled clearly with the name, dose, lot number and expiry date. A copy of the product insert should accompany re-packaged products so that drug distributors and administrators have access to critical information pertaining to the medicine. Products that have been re-packaged should be discarded if not used and never returned to their original containers.

13. **Co-administration of medicines**

Co-administration of NTD medicines is increasingly common for preventive chemotherapy as NTD programmes become more integrated. Co-administration can increase programme efficiency, reduce costs and provide more effective treatment for diseases being targeted.

There are three main types of co-administration. First, for some NTDs, such as lymphatic filariasis, two or three medicines are given together during MDA, since they act synergistically against the filarial parasite. These combinations include ivermectin and albendazole; diethylcarbamazine and albendazole; and ivermectin, diethylcarbamazine and albendazole, also known as “IDA”. Secondly, medicines are combined to target multiple NTDs at the same time. In preventive chemotherapy that addresses both schistosomiasis and soil-transmitted helminthiases, WHO-recommended combinations include praziquantel with albendazole and praziquantel with mebendazole. Thirdly, medicines for NTDs, especially deworming medicines, are commonly administered along with vitamin A, other micronutrients or vaccines during “child health days”.

The disadvantages of co-administering NTD medicines during MDA include the increased risk of mix-ups (particularly if containers are not labelled correctly and tablets appear similar); incorrect dosing; and possibly, choking, if tablets are swallowed all at once. People participating in MDA with co-administration of medicines should be discouraged from swallowing the tablets together (for more information, see module 3, on prevention of choking).
14. **WHO-recommended combinations**

Not all combinations of NTD medicines have been shown to be safe and effective for routine co-administration. As noted in module 1, before WHO recommends co-administration of medicines for treatment of multiple NTDs, such as ivermectin, diethylcarbamazine and albendazole (IDA) for lymphatic filariasis, intensified surveillance for adverse reactions is required in thousands of people to ensure safety. Combinations that WHO recommends can be given together at the same time are shown in green on the slide. The lines in red show other combinations that have been studied and found to be safe and effective in some trials, but WHO has not yet made recommendations pending further evaluations. For example, in research settings in the Western Pacific, azithromycin has been co-administered with ivermectin to target both scabies and yaws, and with IDA to target scabies, yaws, soil-transmitted helminthiases and lymphatic filariasis.

15. **Infection control**

Before the COVID-19 pandemic, little attention was given to minimizing the risk of transmission of respiratory or gastrointestinal infections during MDA. However, lack of proper hygiene, crowding and shared cups or utensils undoubtedly facilitate such transmission.

If MDA is planned during a time when a pandemic, such as COVID-19, is suspected, personal protective equipment, social distancing and other precautions are recommended. Guidance is available from WHO on whether and how to conduct MDA and other community-based health interventions in the context of such settings.

Even in the absence of epidemics of infectious diseases, attention to infection control when administering NTD medicines is warranted.

- If water is used to reconstitute powder for oral suspension or to facilitate swallowing of tablets, it should be clean and given in a way that does not promote cross-contamination.
- Hand hygiene is an important measure for the prevention and control of the spread of disease. If an alcohol-based hand rub is not available, wash your hands with soap and water frequently.
- People with signs or symptoms of a respiratory infection, including health workers, children, caregivers, volunteers and visitors, should cover their mouth and nose when they cough or sneeze, for example “into their elbow”.

16. **Summary**

The safety of interventions against NTDs is absolutely dependent on the safe management of medicines. Safety encompasses a broad range of activities and processes from manufacture to administering the medicine to people who need it. This module has reviewed key steps in safe management of medicines, including manufacture; quality assurance through licensure under stringent regulatory authority or through WHO prequalification; age-appropriate formulation; transport, shipment and storage of medicines; and safe administration. Safe administration involves
creating a safe environment; following exclusion criteria; avoiding re-packaging of medicines; ensuring proper dosing and administration; co-administering only WHO-recommended combinations of medicines; and practicing good infection control.
Module 3: Prevention of choking

1. Welcome

Welcome back to our series of WHO training modules to accompany the manual. These modules are intended to help national programmes for neglected tropical diseases (NTD)s plan, prepare and monitor the safe administration of medicines for treatment of these diseases. This module addresses prevention of choking.

2. Learning objectives

The learning objectives for this module are to:

• know the primary risk factors for choking on medicine;
• be familiar with programmatic and practical steps to prevent choking on medicine given for NTD treatment and control; and
• know what steps to recommend to community drug distributors to prevent choking.

3. Preschool-aged children

Choking – obstruction of the airway – is a significant cause of death in young children.

Although preschool-aged children (that is, children under 5 years of age) do not typically show the clinical manifestations of some NTDs, they can become infected, develop subclinical disease, and contribute to transmission. For this reason, preschool-aged children are included in preventive chemotherapy for trachoma, soil-transmitted helminthiases and lymphatic filariasis (when using diethylcarbamazine and albendazole). A paediatric formulation of praziquantel is under development that will allow the inclusion of preschool-aged children in preventive chemotherapy for schistosomiasis.

4. Choking during mass drug administration

WHO highlighted the problem of choking during mass drug administration (MDA) as early as 2007, when it reported the deaths of four preschool-aged children who had choked when they tried to swallow whole tablets of albendazole. Available evidence suggests that about 1% of young
children experience non-fatal choking during preventive chemotherapy for soil-transmitted helminthiases.

5. **Tablet size and age of child**

The medicines used in preventive chemotherapy are pharmacologically safe. However, some of the tablets are larger in diameter than the trachea (windpipe) of young children. For example, as shown in this slide, the mean diameter of the trachea in a 1-year old child is 5 millimeters, whereas the dimensions of albendazole and mebendazole tablets are considerably larger. If not administered properly, children can aspirate, or choke on, these tablets, blocking the airway. Although fatal choking during preventive chemotherapy is not frequent, it occurs when tablets completely block the airway and cannot be dislodged.

6. **Risk factors for choking**

The major risk factors for choking during MDA include tablet size, young age and forcing children to take tablets against their will. The risk of choking is highest in children aged 1–2 years; it decreases, but does not disappear, above 3 years of age. Indeed, older adults may also have problems swallowing or chewing large tablets.

The most important risk factor for choking appears to be forcing children to swallow tablets when they are crying, in distress, or trying to resist taking the medicine. In one recent study, such children had a 20-fold increase in choking than children who were calm or content.

7. **Choking prevention**

7.1 **Powder for oral suspension**

Choking-related deaths in young children are preventable by giving young children age-appropriate drug formulations, careful planning and training of community drug distributors, and proper drug administration.

For treatment of trachoma, azithromycin is provided as a powder for oral suspension, or POS, which is reconstituted with water and recommended for all children aged under 7 years or less than 120 cm in height, or anyone who has difficulty swallowing tablets. A new paediatric single-dose formulation of mebendazole is now available for treatment of soil-transmitted helminthiases in school-aged children, which creates a soft, easily swallowed mass when combined with a few drops of water; a paediatric formulation of praziquantel for treatment of schistosomiasis is under development.

7.2 **Crushing deworming tablets**

Other medicines commonly used for preventive chemotherapy against soil-transmitted helminthiases (albendazole), lymphatic filariasis, schistosomiasis, and onchocerciasis are available as tablets. WHO recommends that tablets used in deworming (albendazole and mebendazole) be
“broken and crushed” for all children aged under 3 years, and given with water. The risk of choking decreases, but is not eliminated, above 3 years of age. If the crushed tablet is mixed with water, another liquid, or food to encourage the child, care should be taken to ensure that all the crushed tablet is suspended and administered to ensure proper dosing.

Different methods are used to crush the tablets. A WHO document in 2004 recommended crushing tablets between two spoons. It is unclear how widely the recommendation to crush tablets is followed.

7.3 Planning and policy

Prevention of choking must be part of an overall strategy for NTD safety. The push to reach high drug coverage to reduce disease transmission should not override concerns for safety. Children should never be forced to take medicine during MDA in an effort to achieve high coverage. Other characteristics of high-quality programmes that prioritize choking prevention include the following.

- Supervisors of community drug distributors can reinforce the importance of safety and support those distributors who prioritize safety, even if this means that drug coverage is slightly lower.
- Community drug distributors should follow safety precautions for drug administration and be trained, prepared and able to effectively communicate with parents and children. Safety training for should emphasize role-playing, problem-solving, communication and orderly workflow. More detail is provided in the modules for community drug distributors (Annex 3).
- WHO recommends that community drug distributors be familiar with manoeuvres, such as the Heimlich manoeuvre, to dislodge foreign bodies from the airway.
- NTD programmes should periodically conduct observational assessments of MDA to evaluate safety practices and to refine prevention strategies. For example, a recent observational assessment of preventive chemotherapy for soil-transmitted helminthiases found that 12% of children aged under 3 years were forced to take deworming medicine against their will.
- Prompt investigation, management and reporting of serious adverse events are not only legal and regulatory requirements but serve also to decrease rumours, restore trust and sustain high drug coverage. More detail is provided in module 5 on serious adverse events.

7.4 Drug administration

The following guidance is recommended for community drug distributors and others who administer preventive chemotherapy to young children.

- Adhere to the recommended dosing guidelines on dosing and formulation.
- Offer oral suspension for trachoma, or crushed deworming tablets to anyone, of any age, who has trouble swallowing tablets.
- For treatment of trachoma, give azithromycin oral suspension (reconstituted from powder) to all children aged under 7 years or less than 120 cm in height, and to anyone who has
difficulty swallowing tablets. If they are unable to swallow powder for oral suspension or resist taking it, tetracycline eye ointment can be provided.

- For treatment of soil-transmitted helminthiases and lymphatic filariasis, crush albendazole tablets before giving them to children aged under 3 years.

- Directly observe all treatments.

- *Never force* children to take medicine, hold their nose to make them swallow or force their head back to give them the medicine; this increases the risk of choking.

- For children who are fussy, irritable or resist taking medicine, encourage the parent or guardian to calm them so they can receive the treatment.

- If the child continues to resist, *do not* treat the child during this round of preventive chemotherapy.

- When multiple medicines are co-administered during preventive chemotherapy, discourage participants from swallowing all the tablets together at the same time.

8. **Summary**

Fatal choking during MDA is both tragic and preventable. WHO recommends age-appropriate drug formulations for young children. The most important preventive measure is to not force young children to take medicine involuntarily. It is better to be safe and have a slightly lower drug coverage. Preventing choking ultimately depends on the quality of interaction between the community drug distributor and the person taking the medicine (or, in the case of young children, the child’s parent or guardian). Community drug distributors should be trained, prepared and able to effectively communicate with parents and children.
Module 4: Pharmacovigilance

1. Welcome

Welcome back to our series of WHO training modules to accompany the manual. These modules are intended to help national programmes for neglected tropical diseases (NTDs) plan, prepare and monitor the safe administration of medicines for treatment of these diseases. This module addresses collaboration with national pharmacovigilance agencies.

2. Learning objectives

The learning objectives for this module are to:

- understand the benefits of close collaboration with national pharmacovigilance centres; and
- know the several ways of building strong relationships and linkages between NTD programmes and pharmacovigilance centres.

3. Pharmacovigilance

NTD programmes have long recognized the importance of adverse events and serious adverse events associated with NTD medicines. WHO has provided guidance to NTD programmes on investigating and reporting serious adverse events, particularly for events that occur during preventive chemotherapy. In addition to these programmatic efforts, most countries have pharmacovigilance centres, located within or affiliated with the health ministry, which are responsible for drug safety and for investigation, analysis and reports. WHO has also issued guidance for national pharmacovigilance agencies.

4. Parallel systems

The reporting systems for adverse events are not always coordinated between NTD programmes and pharmacovigilance agencies. These systems sometimes operate in parallel and, unfortunately, in isolation from each other. During the early years of NTD control and elimination, NTD programmes often took the lead in reporting serious adverse events. Collaboration with pharmacovigilance agencies was difficult because these agencies are often situated in different governmental departments than NTD programmes, and the capacity of pharmacovigilance programmes to engage with NTD programmes was limited. Furthermore, many pharmacovigilance programmes have had limited experience with MDA.
As NTD programmes have grown in size and are increasingly integrated within health systems, it has become important to collaborate closely with programmes responsible for pharmacovigilance at the national, subnational, regional and global levels. Developing the relationships to support such collaboration may take time and require changes in organizational dynamics or structures, but this is critical for improving the safety of interventions against NTDs within the context of national health systems. Collaboration between NTD programmes and pharmacovigilance agencies has already yielded benefits for NTD control in several countries.

5. Why collaborate?

While stakeholders in NTDs and pharmacovigilance may have different responsibilities and objectives, they often have the same ultimate goals: to improve people’s health and well-being and contribute to a safe and flourishing society. They also share specific aims, including assuring safety, preventing unintended harm, protecting public health, improving the quality of information for decision-making and optimizing use of resources.

By combining forces, both programmes can share responsibilities, increase safety awareness and model the power of collaboration within health ministries. As demonstrated with recent collaboration between the WASH (water, sanitation and hygiene) and NTD sectors, collaboration can enable both programmes to achieve their own specific goals and objectives more quickly and effectively.

The first step in effective collaboration is to define the shared goals and aims among partners.

5.1 Advantages for NTD programmes

The advantages to collaboration for NTD programmes include:

• responsibility for regulatory aspects of medicines that are used in NTD programmes and any necessary collaboration to ensure national regulatory approval and inclusion on the national list of essential medicines;
• specialized expertise in adverse reactions to medicines and their investigation and management, as well as guidance and resources;
• official regulatory authority for addressing serious adverse events;
• awareness of data on NTD-related serious adverse events that are not available to NTD programmes;
• help in demonstrating the NTD programme’s commitment to safety and to cross-sectoral collaboration; and
• expertise and experience in communicating information on risk to communities, which can help increase public trust in NTD programmes.

5.2 Advantages for pharmacovigilance programmes

The advantages to collaboration for pharmacovigilance programmes include:
• proactive collaborative planning that allows for improved safety of MDA as well as management and investigation of serious adverse events, in line with regulatory requirements;
• improved awareness of pharmacovigilance and understanding of simultaneous mass exposure to medication through preventive chemotherapy;
• greater awareness of individual NTD case management, which requires use of medicines with significant side-effects;
• improved analysis of data and timeliness of reporting serious adverse events;
• opportunities to increase awareness on safety of medicines among the public (i.e. the populations served by NTD programmes), which can improve advocacy and support for pharmacovigilance;
• increased opportunity to collect information during investigations of serious adverse events that will directly address efforts to prevent them (e.g. circumstances in which a child choked); and
• more efficient allocation and use of resources as a result of sharing responsibilities with NTD programmes.

6. **How to start collaboration**

Collaboration can start where it is simplest, or easiest to fund, and be expanded at a later stage as a joint work plan develops and resources become available. Simple entry points include:

• seeking out and engaging with a specific counterpart or ally from the pharmacovigilance programme with whom you could collaborate closely;
• inviting pharmacovigilance agencies to NTD meetings, task forces or working groups;
• attending meetings and working groups on pharmacovigilance;
• sharing information on NTD medicines, disease prevalence, drug coverage, and experience with adverse events and serious adverse events;
• identifying potential sources of funding for collaboration and comprehensive programme delivery;
• inviting a representative of the pharmacovigilance agency to participate in national-level NTD training of trainers; and
• adding messaging on pharmacovigilance in NTD training and community sensitization materials.

**Initial meetings**

Collaboration is not just about setting up a coordination structure such as a committee or working group: it requires a team of people working together towards the same goal. Consider a shared achievable goal that the NTD and pharmacovigilance teams work together on. Who should be involved, what expertise and experience do they bring, and to what extent can they commit to being actively engaged over the necessary period?

In an initial series of meetings between both programmes, you may wish to:

• become familiar with each other’s programmes, responsibilities, goals, strategies, objectives and regulatory requirements, with an emphasis on safety;
• discuss implementation challenges that you share in common (e.g. collecting information on details surrounding serious adverse events in a timely fashion; using reports of serious adverse events to develop prevention strategies; addressing community unrest following serious adverse events);
• identify clear opportunities where there is good overlap and measurable results can be achieved quickly;
• identify practical areas where engagement of pharmacovigilance personnel can improve NTD safety and where NTD personnel can facilitate the goals of pharmacovigilance;
• ask pharmacovigilance staff to review messaging by NTD programmes on safety and risk;
• invite pharmacovigilance staff to observe or participate in preventive chemotherapy campaigns;
• begin plans to establish or strengthen working groups or task teams;
• develop and commit to a preliminary scope of work; and
• create a core team responsible for ongoing communication and development of closer collaboration through a situation analysis and a formative assessment of opportunities for collaboration.

7. **Summary**

Pharmacovigilance agencies represent an important resource for NTD programmes, and vice versa. Building smoothly functioning collaborative relationships takes time, but the outcome is well worth the effort. The most important thing is to begin. This module provides suggestions for getting started. Working together, NTD programmes and pharmacovigilance agencies can promote a culture of safety and ensure the health of populations.
Module 5: Serious adverse events

1. Welcome

Welcome back to our series of WHO training modules to accompany the manual. These modules are intended to help national programmes for neglected tropical diseases (NTDs) plan, prepare and monitor the safe administration of medicines for treatment of these diseases. This module addresses the recognition, management and reporting of serious adverse events, also known as SAEs.

2. Learning objectives

The learning objectives for this module are to:

• understand the definition of serious adverse events and the rationale for their investigation and reporting;
• know the criteria for excluding people from preventive chemotherapy with the different NTD medicines;
• be able to prioritize actions when serious adverse events occur;
• understand the principles and elements of adverse event investigations; and
• be able to organize a notification and reporting system for serious adverse events.

3. Adverse events

Despite the pharmacological safety of medications used to treat NTDs, adverse events sometimes occur. The vast majority of these are transient in duration and mild in intensity. Common examples include upset stomach, headache and fever. Some adverse reactions are direct side-effects of the medicines; others are caused by the medicine’s effect on the organism being targeted, particularly for helminths. If patients and communities are well-informed in advance and people who experience adverse reactions know where to seek help, most events can be managed without negative impact on the programme or on the health of individuals. Occasionally, clusters of mild adverse events during preventive chemotherapy can cause panic and disrupt NTD programmes. Concern about adverse events remains a major reason why people refuse to participate in preventive chemotherapy.

4. Serious adverse events

A small proportion of adverse reactions are classified as serious. A “serious adverse event” is a regulatory term describing a medical event that results in death; requires in-patient hospitalization;
results in significant or persistent disability; is life-threatening, or results in a congenital anomaly or birth defect.

Regulations requiring reporting of SAEs were developed for clinical trials and human subjects research, rather than for population-level exposures that occur with public health programmes such as preventive chemotherapy. These regulations require that all serious adverse events be promptly reported to regulatory authorities, regardless of whether they are considered causally related to NTD medicines or interventions.

5. **Adverse events that require investigation and reporting**

Although most adverse events are mild, transient and expected, some adverse events require further investigation and reporting. In addition to SAEs, there are other adverse events that warrant investigation and reporting, even if they do not meet the criteria for SAEs. These include clusters of cases, which affect groups of people, and adverse events that cause significant community concern or disruption, particularly where the cause is unexplained or “operational error” is suspected. Community concern, which may arise even if the medicine is unrelated to the adverse event, is particularly likely in the case of deaths or clusters of adverse events following mass drug administration (MDA).

Investigation and reporting of adverse events alert public health officials to unexpected safety threats and help to quantify the magnitude and pattern of adverse events that are known to be associated with treatment. If properly investigated and analysed, adverse event reports can also contribute to developing strategies and practices to improve NTD safety.

6. **Factors affecting adverse event occurrence**

The frequency of adverse events and serious adverse events varies with the specific medicine(s) being used, the NTD(s) being targeted, and the distribution and prevalence of both targeted and other NTDs in the population. For example, *Loa loa*-related encephalopathy following MDA for onchocerciasis occurs in central Africa, where loiasis is co-endemic with onchocerciasis. For some NTDs such as lymphatic filariasis, onchocerciasis and schistosomiasis, worm burden, or intensity of infection, also contributes to adverse events. Particularly – but not exclusively – in the setting of individual treatment, NTD drugs can interact with other medicines that people are taking, leading to adverse events. As noted in the previous module on prevention of choking, serious adverse events can also result from “operator error” in administering NTD medicines.

Community tensions, conflict and distrust of authorities seem to increase the apparent frequency with which adverse reactions are publicized, particularly clusters of mild, but often dramatic, symptoms that trigger community disruption. Such events, which include episodes of “mass psychogenic illness”, do not meet the criteria for a serious adverse event, but they attract considerable media attention and can threaten community acceptance of NTD programmes.

The settings in which serious adverse events are detected and the routes through which they are reported to regulatory authorities may differ among NTDs addressed through preventive chemotherapy and those that require individual treatment. For example, SAEs following individual
treatment in clinics or hospital settings are more likely to be recognized and reported by attending physicians than community health workers.

7. **Serious adverse events and MDA**

Serious adverse events are of particular concern in the context of MDA, since entire populations – including people who are healthy and not affected by NTDs – are presumptively treated. Reporting of such events has identified two major safety issues associated with preventive chemotherapy. First, SAE reports from Central Africa during MDA with ivermectin for control of onchocerciasis led to the recognition that coinfection with *Loa loa* was responsible for unexpected cases of encephalopathy and coma, as well as to a series of research studies and efforts to prevent and improve the outcome of these cases. Secondly, reports of fatal choking led to WHO recommendations that young children receive crushed, rather than whole, tablets, and that they not be forced to take medicine while crying or resisting.

Much less frequent are cases of Stevens–Johnson syndrome, a serious skin condition sometimes associated with certain medications, and seizures in people with neurocysticercosis who receive praziquantel for schistosomiasis or taeniasis, or albendazole for soil-transmitted helminthiases, lymphatic filariasis or taeniasis.

8. **Exclusion criteria during MDA**

Many serious adverse events can be prevented by adhering to recommended criteria for exclusion from treatment. Individuals with serious illness should be excluded from preventive chemotherapy because they are more likely to experience adverse health events in general (related to their illness, not to drug ingestion) and because any drug-related adverse events they experience are more likely to be serious. Seriously ill individuals are defined as those who:

- have an illness that makes them too sick or weak to get out of bed: or
- are currently hospitalized.

Additional general exclusion criteria include:

- young age (the lower eligible age varies for different medicines).
- pregnant women (with exceptions);
- people with diagnosed with neurocysticercosis or a history of seizures or epilepsy; and
- people who have previously suffered from serious adverse events caused by a reaction to the medicine, such as Stevens–Johnson syndrome.

9. **Adverse events and individual treatment**

For some NTDs that are not suitable for preventive chemotherapy, effective treatment requires multi-day courses of medicines that are administered in clinical settings by experienced medical personnel, with careful monitoring for toxicity. These diseases include visceral leishmaniasis, human African trypanosomiasis, Chagas disease, Buruli ulcer, leprosy or Hansen’s disease, neurocysticercosis and echinococcosis (see Table 5 in the manual).
Treatment for these diseases should always be administered by trained personnel, following recommended protocols for drug administration and adverse event monitoring. Adverse events commonly associated with these medicines are listed in Table 5 of the manual.

10. Adverse events commonly associated with NTD medicines not used in preventive chemotherapy

Reliable data on adverse reactions associated with treatment for these NTDs comes largely from clinical studies rather than population-level adverse event reporting. WHO regional NTD officials anecdotally report that serious adverse events are commonly reported for treatment of visceral leishmaniasis and leprosy, which likely reflects the number of people treated, the duration of treatment and the toxicity profile of the drugs.

Preventive chemotherapy with niclosamide is being considered for prevention of *Taenia solium* taeniasis and neurocysticercosis; post-exposure prophylaxis, a form of targeted preventive chemotherapy, is recommended for leprosy, using single-dose rifampicin. Data on the safety of these drugs in mass treatment are more limited than for other NTD medicines commonly used in MDA.

11. Getting prepared for serious adverse events before MDA

A rapid, professional and effective response to SAEs is possible only with advance planning and preparation, which should involve all levels of the health system as well as communities.

- Community drug distributors, health workers and district health officers should all be familiar with, and able to rapidly recognize, SAEs associated with different NTDs and NTD medicines.
- A chain of reporting should be agreed upon and rehearsed in advance, and provisions made to notify and seek immediate help from the appropriate health officials should such events occur. Their telephone numbers should be made available to all NTD programmes. District health officers should know who to contact at the national level for immediate assistance, and they should all have the appropriate SAE reporting forms and know how to fill them out (see section below on reporting forms).
- National and subnational pharmacovigilance agencies should be informed in advance of preventive chemotherapy, including the location, dates, medicines used, diseases targeted and estimated number of participants.
- The community, or in the case of individual treatment, the patient, should be informed about the possibility of adverse events as well as where they should seek help if these events occur. Such communication generates trust and demonstrates concern for high-quality people-centred care, a core element of universal health coverage.
- Particularly in the setting of MDA, in which people participate for the benefit of the community, public health programmes have a “duty to care” for people who experience adverse events and serious adverse events. A national policy should be in place that specifies who will be responsible for their care.
- Further details about preparing for MDA are provided in module 6, on communication.
12. What to do when serious adverse events happen during MDA

12.1 First priority for action

The immediate priority in responding to SAEs is to provide care for the patient and reassure the community. In settings of preventive chemotherapy, community drug distributors should have immediate access to supervisors or district health staff to arrange for referral and medical care as needed.

12.2 Second priority for action

A second urgent priority in response to SAEs is communication, which must be based on known facts and occur quickly, smoothly and at multiple levels. Patients and their families must be reassured that they are safe and being cared for. Community members and the media must be provided with accurate information to prevent the spread of rumours and misinformation, which can harm NTD programmes. Health and regulatory officials must also be notified, both to provide necessary medical care and to initiate appropriate response and investigation. NTD programmes should have a communications plan that can be activated in the case of SAEs. For more information, see module 6, on communication.

12.3 Other priorities for action

In addition to caring for the patient and communicating effectively, effective response to SAEs includes (i) notifying all people who need to be informed; (ii) investigating the circumstances and causes of the SAE; and (iii) reporting the findings to health and regulatory officials.

13. Chain of notification

In addition to a general communications plan, NTD programmes should have a clear plan for who should be notified, and within what timeframe, when adverse events occur. These plans should be developed in collaboration with national pharmacovigilance centres. Most adverse events that are expected, mild and transient can be managed by community health workers. District health officers, NTD programme personnel and pharmacovigilance agencies should be notified if reactions are more severe or are of concern to the community, so they can provide care, share information, conduct appropriate investigations and file necessary reports. In general, SAEs must be reported within 24 hours to WHO, regulatory agencies and pharmaceutical manufacturers, particularly if the medicines are donated. Because severe or serious adverse events occur infrequently, these notification plans should be reactivated and rehearsed before each MDA.

14. Investigation of adverse events

14.1 Conduct of investigation

Soon after an adverse event occurs, an investigation should be conducted if the adverse event (i) is a serious adverse event; (ii) involves a cluster of cases; (iii) causes significant concern or disruption;
(iv) is likely due to operational error; (v) is unexplained; or (vi) is otherwise required by national regulations.

Typically, investigations are conducted by national and subnational health and regulatory officials who interview witnesses, review the chain of events that led to the SAEs, and assess whether the adverse event was causally related to NTD medicines. They may send samples of the medicine(s) used during preventive chemotherapy to a reference laboratory be tested for quality and purity. These officials submit a standardized report, conforming with WHO specifications, to national NTD programmes and pharmacovigilance agencies, pharmaceutical companies and international regulatory agencies.

14.2 Purpose of investigation

The investigation serves several purposes. National and international regulatory authorities require an investigation and reporting of all serious adverse events. Investigations also serve to reassure the community that NTD programmes take any threats to MDA safety very seriously. Even though most SAEs are not directly caused by NTD medicines, investigations are important to identify the cause. Finally, investigations, if properly conducted, can help to identify opportunities for prevention and improving programme performance.

15. Reporting serious adverse events

The chain of reporting serious adverse events follows that for notification (above). SAE reports are sent by NTD programmes and regulatory agencies to stakeholder organizations, including WHO, pharmaceutical companies and international regulatory agencies. National pharmacovigilance centres forward reports on all SAEs (not only those related to NTDs) to the WHO Collaborating Centre in Uppsala, Sweden, where they are further analysed.

Standardized forms have been designed to systematically record and report the findings of investigations on serious adverse events. They serve an important regulatory function and provide consistent information to all key stakeholders. Each country has its own SAE report forms, but the core information is similar, and includes information on patient demographics; the NTD(s) being treated; medicine name, manufacturer, and lot number of the medicine(s) ingested; and circumstances of the SAE. An example of a national SAE report form is shown in the slide.

16. Specialized investigations and reporting forms

Despite their advantages, standardized forms provide inadequate information on features of adverse events that may be important for the control or elimination of specific NTDs. More detailed information, which is important for certain NTD programmes, is collected using ancillary forms. For example, leprosy control programmes collect additional clinical information on immunological “type I and type II reactions” in response to treatment. Effective management and prevention of these reactions is important for preventing leprosy-related disability, a key goal of the WHO Global Leprosy Programme.
In addition, NTD programmes may need more detailed information to determine risk factors and identify prevention opportunities for specific SAEs, such as choking. For example, to develop and evaluate prevention strategies for choking in young children, information should be gathered during the investigation on formulation (e.g. tablet or oral suspension) and form (e.g. crushed or whole tablet); whether the child was forced to take the medicine while resisting or crying; the position of the child (i.e. upright or supine); who gave the medicine (i.e. health worker, parent or the child herself); and whether the treatment was observed by a community drug distributor or health worker. An example of a draft ancillary form for choking-related events is available in Fig. 2 of the manual.

17. Planning for adverse events

As with other aspects of safety, advance planning is essential to properly identify, manage, investigate and report adverse events. In addition to the planning steps highlighted above, which emphasize close collaboration between NTD programmes and national pharmacovigilance centres, the following actions are recommended.

- Reports of adverse events, as well as unofficial accounts of rumours, should be jointly reviewed by the national NTD programme, the NTD task force and the national pharmacovigilance centre at least annually, with a view towards prevention. At the regional and global levels, these events should also be reviewed and discussed by WHO regional offices and headquarters, NTD medicine donation programmes, donating pharmaceutical companies and responsible regulatory agencies.

- Each national NTD programme, in collaboration with the national pharmacovigilance centre, should undertake an analysis of SAE reports associated with treatment for NTDs and should update this analysis periodically to identify trends and opportunities for prevention.

- Based on these reviews and analyses, NTD programmes, in collaboration with pharmacovigilance centres, should determine priority adverse events areas for ancillary data collection and prevention, and develop the necessary investigational and reporting processes and forms.

18. Summary

Managing adverse events properly is essential for maintaining confidence in NTD programmes, both for MDA and individual treatment. Even though serious adverse events occur infrequently, when they do occur, they can have a significant and negative effect on NTD programmes. It pays to be prepared.

This module summarizes information on identifying, managing, investigating and reporting adverse events. Additional detail can be found in the WHO document on assuring the safety of preventive chemotherapy for the control of NTDs and an associated handbook. Programme managers should consult these documents for further information and guidance.
Module 6: Communication

1. Welcome

Welcome back to our series of WHO training modules to accompany the manual. These modules are intended to help national programmes for neglected tropical diseases (NTDs) plan, prepare and monitor the safe administration of medicines for treatment of these diseases. This module addresses communication.

2. Learning objectives

The learning objectives for this module are to:

- understand the importance of informed consent in treatment and prevention of NTDs;
- be familiar with the elements of an NTD communication plan;
- be familiar with basic principles for communicating with the media; and
- understand the importance of rapidly and effectively addressing rumours and misinformation related to preventive chemotherapy.

3. Communication and NTD control

Communication has long been recognized as essential by NTD programmes to ensure compliance with and acceptance of preventive chemotherapy by communities. Effective communication is also necessary to optimize treatment of individual patients with NTDs in order to enlist their compliance with medication and other measures. Both for preventive chemotherapy and for individual treatment, effective communication begins with listening to the concerns of those receiving treatment.

Even experienced NTD programme managers express an ongoing need for preparedness, training and practice with communication. For preventive chemotherapy, communication is required at multiple levels – individual, community and the media – and at different times: before, during and after mass drug administration (MDA). Effective communication is challenging for several reasons. Recent growth in the number of people participating in preventive chemotherapy, some for the first time, may contribute to increased numbers of adverse events. In addition, as NTD programmes succeed in reducing the prevalence of infection and disease, the need for MDA becomes less obvious to communities. Furthermore, the relative infrequency of serious adverse events makes it difficult to
communicate effectively when they do occur. The political and social context in which MDA takes place must also be taken into consideration when planning and delivering MDA communications.

4. Individual treatment

Communication is essential to obtaining informed consent, which is an ethical requirement for both research and medical treatment. In many societies, informed consent may involve the community as well as the individual. For example, individuals may not agree to treatment if their village chief or the head of the household has not been asked.

Effective communication begins with questions that elicit the concerns of the patient and the family. Important messages before and during treatment include basic information on the disease and its progression; the rationale for treatment; information on the medicine, its benefits and safety; what to expect with treatment; and how to get help, if needed. The patient should understand the treatment plan and be able to ask questions about it.

Ongoing communication is crucially important during the course of treatment to detect problems with medication or other interventions and to make appropriate adjustments promptly. Communication is also important when treatment is concluded, since patients may have questions about what to expect, whether follow-up is needed, and how they can get help, if needed.

5. Preventive chemotherapy communication

5.1 Communicating with communities before MDA

Communication is essential for community mobilization and high drug coverage with preventive chemotherapy. At the community level, community health workers and drug distributors should be trained to share information about the disease being targeted; the safety and effectiveness of the medicines that will be used in preventive chemotherapy, and the risk of specific adverse reactions. This should include messages on where and how to seek care for adverse reactions if they occur, and it may require tailoring message to different groups within the community. This information can be shared through social media, written materials and meetings with community leaders. As with individual treatment, careful listening to the concerns of community members and addressing rumours is an important part of communication at the community level.

5.2 Communicating with the media before MDA

The second crucial audience for communication in advance of MDA is the media, including social media. Establishing relationships with reporters and media personnel well in advance of preventive chemotherapy will be helpful for enlisting their help to promote MDA, encourage community participation and convey accurate information about the timing of treatment, as well as the potential for adverse reactions. The media can instill trust and foster community participation or generate distrust and disrupt MDA. Communicating effectively with the media requires training and practice.
In recent years, social media has become a crucial communication tool for NTD programmes. Effective mobilization of social media may include enlisting “influencers” (people who have large followings on social media) to disseminate accurate messages through various social media channels and SMS text messaging; employing “listeners” to follow the chatter on social media and detect any distortion or deviation of messages; and the ability to respond effectively and rapidly to mitigate negative effects on the programme.

During planning for the MDA, NTD programmes should designate a spokesperson who receives training in speaking to the press, including practice addressing questions and inquiries from the press in different scenarios. This person or a member of the team should also be trained in use of social media. NTD programmes should also develop a communications plan that helps to mobilize the community and engage community leaders before treatment; provides updated information and encouragement during MDA; and shares information after MDA is concluded. All programme officials should be familiar with key messages. Draft press statements for the most common scenarios (which can be edited as needed for specific events) should be prepared before MDA, particularly to address the occurrence of serious adverse events and to quell rumors. Close collaboration with and involvement of the national pharmacovigilance agency in developing communications in the event of an incident can help to generate public confidence and trust and reinforce preparedness for adverse events.

6. Communication in the context of adverse events and rumours

If an adverse event occurs that affects the health of individuals receiving NTD medicines or threatens the programme, the immediate priority is attending to the patient and ensuring that they receive appropriate medical attention. Community drug distributors, health workers and, for school-based programmes, teachers, should know who to contact for assistance and have ready access to that person. Compassionate, professional and calm communication with the patient and family members is essential.

A second urgent priority is to communicate with the community and the media to provide essential information, restore trust, and counteract misinformation and rumours. Regardless of whether the event is truly related to the MDA or only perceived to be, it can become a crisis if not managed properly or planned for in advance. The “listening” part of communication is especially important in the setting of a serious adverse event in order to communicate effectively the issues that matter most to the community. Establishing a “rumour inventory” that is reviewed every day is a good way to adapt communication messages to address the concerns of the community and to effectively communicate factual information.

7. Communicating with the media when adverse events occur

Communication skills are never more important than when panic erupts in communities or in the media following adverse events, even when those events are not caused by NTD medicines. Recommended steps for effective communication in such settings adverse events include the following.
• Activate the communication plan and adapt it to the current crisis.
• Activate social media channels to counter rumours and provide accurate information (see section below).
• Identify a spokesperson to interact with the media (consider geographical location of the serious adverse event, the language of those affected, and engagement of the respected community and health leaders).
• Define the audiences that need to receive information (there may be several, e.g. public, media, community leaders, health professionals).
• Identify delivery mechanisms for each major audience (e.g. in-person meetings, radio, newspaper, television, social media).
• Design a few simple key messages for each audience, which may include the following:
  − concern and empathy for the person experiencing the serious adverse event;
  − reassurance that the incident is being taken seriously and is under investigation;
  − emphasis of the overall excellent safety track record of NTD medicines globally;
  − confirmation that the medicines are of assured quality (provided this is true);
  − reassurance that safety is a chief concern of the programme and that a reporting system (surveillance) has been established to detect, manage and prevent serious adverse events;
  − confirmation that the investigation will address the causes or factors contributing to the serious adverse event so that it can be prevented in the future (give specific examples);
  − reassurance that many serious adverse events are coincidental, i.e. the event is not causally related to the medicine or its administration.

8. **Tips for effective communication by the spokesperson**

The designated spokesperson (as well as other authorities who may be called upon) should be prepared to communicate effectively, respond appropriately to difficult questions, and convey a sense of trust, competence and concern. He or she should prepare answers in advance and practise for the likely and awkward questions.

The following tips may be helpful.

• Project a strong, compassionate, competent image for yourself and the NTD programme.
• Identify which issues not to respond to (e.g. blaming an individual or speculating on the cause before the investigation is complete).
• Be honest. Never lie. If you do not know, say so, but promise to find out (e.g. “We do not know at this time, but we have taken steps to answer that question”).
• Avoid improvisation and casual remarks. Be serious: jokes can be disastrous. Avoid jargon; use simple phrases and give examples to clarify your meaning.
• Be aware of body language, which is critically important for perceptions. Practise in advance can be particularly helpful to increase self-awareness of body language.
• Be **responsible**: do not be defensive; accept responsibility appropriate to your position.
• Be **responsive**: hold a daily press conference if that is what is needed to meet the needs of the public and the media; regular contact helps build a trusting relationship with the media.

• Be **positive**: reframe the situation in positive terms; use terms such as “safety” (which has a positive connotation) rather than “adverse event” (which can be construed negatively).

9. **Techniques when faced with a hostile interviewer**

When facing a hostile interviewer, be prepared to use these “ABCD” techniques:

- **Assure**: Respond to a negative question with a positive answer (e.g. when asked, “How many children have died from preventive treatment?”, answer: “Preventive chemotherapy saves lives. Since our programme began, X children have been treated, and of them Y% might have died from one of these diseases. That is the context in which we must consider the tragic, but thankfully rare adverse events which follow preventive chemotherapy.”)

- **Bridge**: Having answered a difficult question, move to something linked but positive.

- **Correct what is wrong**: Immediately correct information from the interviewer that is wrong.

- **Deliberate**: Take time to think about your response to questions. Do not be rushed or forced. Be deliberate.

10. **Approaches to using social media to counter rumours and misinformation**

Effective use of social media has become a crucial asset for countering rumours, providing accurate information and allaying community concerns. Competency in social media should now be an essential part of a communications strategy for NTD programmes. A few key principles are suggested here.

First, become educated on the social media platforms in your area, the audiences they reach and influence, and the issues they address. Identify which of these platforms are most likely to spread rumours and misinformation, and which will be the most influential for countering them. As part of the communications plan, establish a presence on these platforms and cultivate relationships with “influencers”. Secondly, determine what types of rumours and misinformation pose the greatest threat to the NTD programme, and develop and test different responses. For example, for certain kinds of rumours, or misinformation circulated among particular groups, it may be more effective not to respond to or acknowledge the rumour, which could only draw further attention to it. In other situations, a strong response with accurate information, particularly if delivered or supported by influencers, may be the most effective. Thirdly, ongoing “listener” surveillance should be established for health-related misinformation that may impact the NTD programme. Finally, social media should link with and direct the public to the website of the NTD programme or the Ministry of Health, or to other reliable sources, where more detailed information can be provided. Preparedness and a rapid, coordinated approach to rumours and misinformation are increasingly necessary as social media has become such a dominant source of news and information.
11. **Summary**

Communication at multiple levels is essential for safe NTD programmes, from the individual to the community and to the mass and social media. Communication is essential before, during and after treatment. Communication becomes crucial if serious adverse events or rumours occur during MDA.

Effective communication is a skill that can be learned and requires practise. NTD programmes should have a communications plan that provides guidance during MDA planning and can be immediately activated in the case of adverse events.